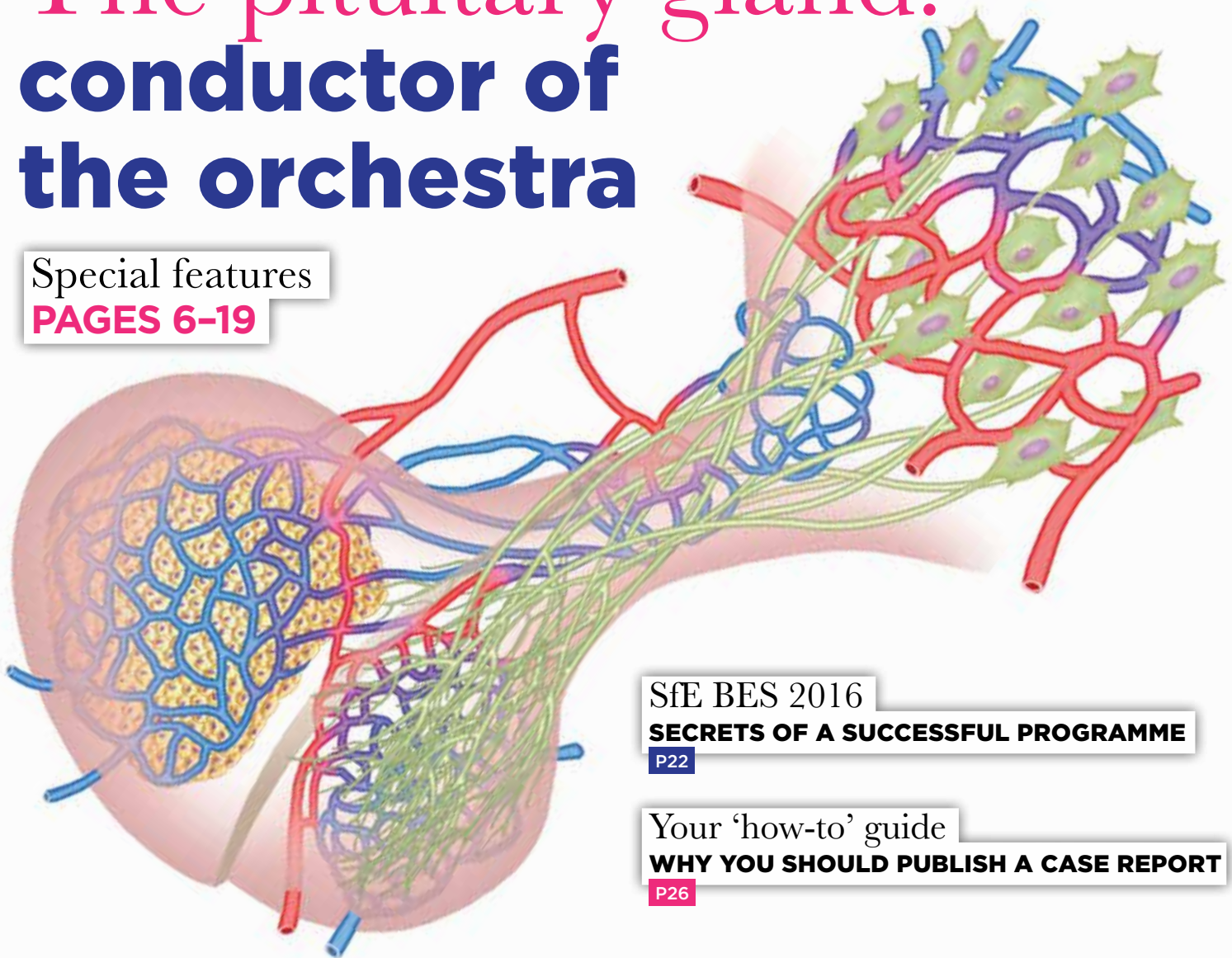


THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

The pituitary gland: conductor of the orchestra

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A word from THE EDITOR...



It is with a mixture of a heavy heart and sense of pride that I write this last of my editorials (calm down dear, it's only *The Endocrinologist*). Welcome to this year's winter edition, which contains a festive endocrine stocking full of pituitary delights. I have been self-indulgent with the theme – the pituitary gland is the endocrine organ closest to my heart (anatomically a dubious statement I know). Inside are articles on the embryology and pathology of the pituitary, as well as the non-classical roles of prolactin. Simon Cudlip has written an autobiographical account of his path to becoming a pituitary surgeon (it's been a journey). We have brilliant articles on pituitary radiotherapy, the role of PET scans in pituitary disease, and a Xmas special of famous celebrities with pituitary conditions. As always we are grateful to those who have taken time out of their busy lives to write for us.

So, as the nights draw in and the Sherlock Xmas special approaches, we can reflect on another year gone by. The wider world appears increasingly unstable, but we are safe in the knowledge that our own little endocrine world is thriving. The Society's BES conference was a great success and there is much to look forward to in the endocrine calendar of 2016.

I am genuinely pleased and flattered to have been involved in this magazine for the last five years. It is in very good hands with Tony Coll taking over the reins. I am planning to continue the interviews – I think hearing the human stories of our greatest exports brings us closer together in some way. Have a restful Christmas and New Year, and as they say in *The Apprentice* – thanks for the opportunity!

BEST WISHES

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Become a contributor... Contact the Editorial office at endocrinologist@endocrinology.org

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the Spring 2016 issue: **1 December 2015**.
Deadline for news items for the Summer 2016 issue: **21 March 2016**.

Front cover image ©SHUTTERSTOCK



We wish all our readers a very merry Christmas and happy new year



DON'T FORGET: RENEW YOUR MEMBERSHIP!

Membership for 2016 commences on 1 January. If you already have a direct debit mandate in place, there is no need to do anything – your membership will be automatically renewed on 1 January 2016.

If you don't yet have a direct debit set up, call the Membership Team today on +(44) 1454 642 202, or email members@endocrinology.org

To find out more about the benefits of joining the Society for Endocrinology, visit www.endocrinology.org/membership

COUNCIL AND COMMITTEE MEMBERS

The recent AGM saw a number of changes to Council:

Graham Williams became President elect, and will take over from Stephen O'Rahilly when his term of office finishes at the next AGM.

Karen Chapman has replaced David Ray as General Secretary.

Barbara McGowan has replaced Graham Williams as Treasurer.

Simon Pearce has replaced Chris McCabe as Programme Secretary.

We thank the retiring Officers and three other Council members who are stepping down: Jonathan Seckl, Tony Weetman and Anne White. They are replaced by Ruth Andrew, Mark Gurnell and Martin Hewison.

Our thanks are also due to three Committee Chairs who will step down at the end of this year, Karen Chapman (Science Committee), Samantha Mirczuk (Early Career Steering Group) and Saffron Whitehead (Public Engagement Committee), as well as all the Committee members who are completing their terms.

We welcome and look forward to working with the new Committee Chairs: Chris McCabe (Science Committee), Maralyn Druce (Public Engagement Committee) and Anna Mitchell (Early Career Steering Group).

If you would like to have a say in how your Society is run, please consider standing for election via the call for nominations that will appear in the next issue of *The Endocrinologist*.

WEBSITE UPDATE

Development of the new Society for Endocrinology website continues apace. We've been working on new page layouts to make it easier to find the information you need, as well as introducing some fresh features you told us you'd like to see. The overall design has been updated and we're now busy building and testing before we launch next year. Many thanks to our members who have given us valuable feedback!

CONGRATULATIONS

Society member Ruth Andrew has been appointed Chair of Pharmaceutical Endocrinology at the Edinburgh Clinical Research Facility.

Society member Andrew Hattersley (Exeter) has been awarded the 2016 Royal Society GlaxoSmithKline Prize and Lecture for his work on genetic and physiological studies of individuals with common subtypes of monogenic diabetes, revolutionising treatment for these patients.

Society President Stephen O'Rahilly (Cambridge) has been awarded the inaugural European Association for the Study of Diabetes Novo Nordisk Foundation Prize for Excellence.

CHANGES AT THE ENDOCRINOLOGIST



Tony Coll and Miles Levy

Changes are afoot at *The Endocrinologist*, with Miles Levy (Leicester) finishing his term of office as Editor at the end of this year. Miles has worked tirelessly over the past three years to improve the quality and content of the magazine, ensuring it is relevant and appealing to Society members. We're incredibly grateful for all the enthusiasm, tenacity and drive he put into this role. From January, the role of Editor will pass to Tony Coll (Cambridge) who currently holds the post of Associate Editor. Amir Sam (London) will join the team at this time as the new Associate Editor.

Our grateful thanks also go to retiring Editorial Board members Paul Foster (Birmingham) and Paul Grant (Brighton) for all their input and hard work over the last 3 years. We look forward to welcoming Kim Jonas (London) to Editorial Board from January.

SEEKING VOLUNTEERS

We have a packed programme of public events in 2016 and we're looking for volunteers to help us develop and deliver activities. From science fairs to debates to music festivals, we will be talking about hormones with a huge range of under-18s, families and adults.

For more information, please email Fiona Docherty at fiona.docherty@endocrinology.org.

You can read one volunteer's experience on page 24.

SOCIETY CALENDAR

2 February 2016
NATIONAL CLINICAL CASES
London

26-28 February 2016
CAREER DEVELOPMENT WORKSHOPS
Warwickshire

21-22 March 2016
ENDOCRINE NURSE UPDATE
Birmingham

21-23 March 2016
CLINICAL UPDATE 2016
Birmingham

see www.endocrinology.org/meetings for full details

GRANT AND PRIZE DEADLINES

15 DECEMBER 2015
TRAVEL GRANTS

11 FEBRUARY 2016
STUDENT ESSAY PRIZE

11 MARCH 2016
SUMMER STUDENTSHIPS

15 MARCH 2016
TRAVEL GRANTS

15 APRIL 2016
REGIONAL CLINICAL CASES MEETING GRANTS

27 MAY 2016
EARLY CAREER GRANTS

27 MAY 2016
EQUIPMENT GRANTS

see www.endocrinology.org/grants for full details of all Society grants



SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the members' area on the Society home page, www.endocrinology.org. *Endocrine Connections* and *Endocrinology, Diabetes & Metabolism Case Reports*, the Society-endorsed case reports publication, are open access (OA) and free to all.



JOURNAL OF ENDOCRINOLOGY

Learn to love lipids all over again

To some, the world of lipid biology starts and finishes with the annual process of ticking a box to make sure the patient is on a statin. However, to understand the mechanisms underpinning lipid pathology requires an insight into the dynamic processes of absorption, synthesis and breakdown.

In a well-paced and clearly set out article, Margot Umpleby tells you all you ever wanted to know about the world of stable isotopes and lipid metabolism but

were afraid to ask. From the role of dynamic isotope dilution in the assessment of whole body production rates, to using tracer conversion as a measure of fatty acid oxidation, both theory and practice of modern measurement of lipid biology are deftly covered.

In an era when physiological studies centred on human subjects are increasingly on the wane, this guideline article serves as a timely primer.

Read the full article in *Journal of Endocrinology* **226** G1–G10 (OA)

JOURNAL OF MOLECULAR ENDOCRINOLOGY

IL6 and tamoxifen resistance in ovarian cancer cells

The prognosis of ovarian cancer remains poor, with an estimated 5-year survival of around 50%. Although 40–50% of these cancers express oestrogen receptor α (ER α), in contrast to breast cancer, only a very small proportion respond to tamoxifen.

Interleukin 6 (IL6) has been shown to have a role in development and progression of ovarian cancer, and high levels are associated with a poor prognosis. Using four ovarian cancer cell lines that secrete different amounts of IL6, Wang *et al.* demonstrated that tamoxifen resistance correlated with

IL6 levels. Further investigation and manipulation of IL6 secretion by these cells indicated that IL6 phosphorylated ER α at Ser116 and Ser167 by activation of MEK/ERK and PI3K/Akt signalling, and that cross-talk between oestrogen and IL6 signalling may exist.

Manipulation of immune responses, in particular increased immune surveillance, in the prevention and modification of cancer progression offers exciting treatment possibilities. This study suggests that the effectiveness of tamoxifen might be enhanced by targeting IL6 as well.

Read the full article in *Journal of Molecular Endocrinology* **54** 351–361

ENDOCRINE-RELATED CANCER

Androgen receptor in PTEN inactivation-induced uterine cancer

Mutations in the tumour suppressor phosphatase and tensin homologue (PTEN) result in Cowden syndrome, a rare autosomal dominant inherited disorder characterised by multiple tumour-like growths called hamartomas and an increased risk of developing hormone-dependent cancers. PTEN mutations are commonly observed in uterine cancers, although their cause is poorly understood. Although uterine cancers respond strongly to oestrogen and progesterone signalling, how androgens potentially affect them is unclear.

Choi *et al.* examined whether complete androgen receptor (AR) knockout impacts uterine abnormalities and carcinogenesis in PTEN-deleted mice.

PTEN knockout animals exhibited numerous uterine pathologies that were significantly reduced in combined heterozygous PTEN and AR knockout mice. This effect may involve oestrogen receptor (ER) signalling, as reduced stromal ER α was noted in the uteri of PTEN knockouts compared with the double PTEN/AR-deleted animals, suggesting cross-talk exists between AR and ER α in uterine tissue.

These data provide the first *in vivo* evidence that androgen signalling may be important in uterine cancer development, and that anti-androgens might be novel therapies for prevention of and in early-stage uterine cancer.

Read the full article in *Endocrine-Related Cancer* **22** 687–701



ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

GR transrepression may inhibit bladder cancer growth

Evidence indicates that the glucocorticoid receptor (GR) has a role in reducing urinary bladder cancer cell growth and invasion. In contrast, androgen receptor (AR) activation appears to induce tumour progression.

Compound A is synthetic analogue of a plant aziridine precursor that modulates GR action, but antagonises the AR. Zheng *et al.* utilised several human urothelial cell lines and a mouse xenograft model to investigate the actions of compound A (in comparison with dexamethasone and hydroxyflutamide) on bladder cancer growth and invasion. A range of assays (proliferation, apoptosis, colony forming, cell migration and invasion, gene analysis) were used to assess the impact on cell growth and invasion. Compound A inhibited proliferation, promoted growth arrest and apoptosis and reduced cell migration. Xenograft size was also reduced. Key elements of nuclear factor (NF) κ B signalling were modulated, indicating that compound A may reduce bladder cancer cell growth by mediating GR transrepression.

This suggests compound A may present an alternative treatment for bladder cancer compared with individual GR ligands or AR antagonists.

Read the full article in *Molecular Endocrinology* **29** 1486–1497

CLINICAL ENDOCRINOLOGY

The natural history of subclinical hypothyroidism

Subclinical hypothyroidism, as defined by an elevated thyrotrophin (TSH) level with a normal free thyroxine (T₄), can prove a diagnostic conundrum, particularly when accompanied by non-specific symptoms of fatigue or weight gain. There is some evidence that such patients benefit from treatment if TSH exceeds 10mU/l.

Rosario *et al.* evaluated the natural history of 252 women in Belo Horizonte, Brazil, with subclinical hypothyroidism and TSH levels ranging from 4.5 to 10mU/l, over a period of 5 years. Serum antithyroid peroxidase antibodies

(TPOAb) were measured in all the patients in this prospective study, with an ultrasound scan of the thyroid if this was negative.

Overt hypothyroidism developed in 19% of patients, while in 23% the TSH spontaneously normalised. The remainder continued to meet the criteria for mild subclinical hypothyroidism. The only predictor of the need for treatment with L-T₄ was TSH >8mU/l, although an absence of signs of thyroiditis (TPOAb positivity or ultrasound characteristics) predicted TSH normalisation.

Read the full article in *Clinical Endocrinology* doi:10.1111/cen.12939

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Transient diabetes insipidus in pregnancy

Gestational diabetes insipidus is a rare pregnancy complication, occurring in 2–4 out of 100,000 pregnancies. It generally appears in the third trimester, resolving at 4–6 weeks post-partum.

Marques *et al.* report a 38-year-old woman, admitted to hospital in the 37th week of her first single gestation, suffering from polyuria, nocturia and polydipsia. Gestational diabetes mellitus had been diagnosed in her second trimester, but otherwise her medical history was unremarkable. Tests showed low urine osmolality (89 mOsmol/kg; 350–1000). No water deprivation test was performed due to the risks of dehydration in pregnancy.

The patient was diagnosed with gestational diabetes insipidus and immediately started on desmopressin, which improved her symptoms and normalised serum and urine osmolality. She gave birth at 39 weeks without major problems.

Following delivery, desmopressin was stopped after 8 weeks without return of symptoms. A magnetic resonance imaging scan at 12 weeks post-partum revealed normal pituitary anatomy. The patient continues to be clinically well, breastfeeding and off all medication.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* 10 doi:10.1530/EDM-15-0078 (OA)

ENDOCRINE CONNECTIONS

Pre-eclampsia and infant postnatal cortisol metabolism

Pre-eclampsia occurs in approximately 3% of pregnancies and, amongst other effects, can cause a decrease in the pituitary-adrenal feedback mechanism present in the fetus.

Broughton Pipkin *et al.* set out to determine if this disruption leads to long term effects on glucocorticoid metabolism in the infant at 3 and 12 months of age. Cortisol metabolites and apparent enzyme activities were analysed by gas

chromatography-mass spectrometry of urine samples taken from 3-month-old infants ($n=95$) and 12-month-old infants ($n=45$).

They found that infants born to mothers who had pre-eclampsia exhibited an increase in 11 β -hydroxylase at 3 months, which appeared to compensate for the high 11 β -HSD-dependent cortisol degradation. This increase was still evident at 12 months of age, where it appeared to counterbalance reduced cortisol substrate availability.

Read the full article in *Endocrine Connections* doi:10.1530/EC-15-0084 (OA)



'It ain't what you do, it's the way that you do it...'

Model organism studies suggest restricting the time window in which eating occurs, without affecting quantity or quality, can be highly beneficial. This may also be true for humans, but studies of food consumption are hampered as self-reporting techniques are prone to reporting bias.

Gill & Panda used a mobile app to show that modern humans do not eat two meals a day in a 12-h period, but have a far more erratic pattern. More than half the adults studied ate over 15-h or longer, making time in the post-prandial phase far longer than any fasting period. Breakfast has disappeared for most, with a bias towards consuming the majority of the caloric intake towards late afternoon and evening.

In a small pilot study, eight subjects with a >14-h eating duration received biofeedback as a 'feedogram' to their phone. This led to a reduction in their caloric-containing eating duration to between 10 and 12 h, resulting in an average loss in weight of >3kg and better quality sleep. Checking your phone relentlessly may be good for your health!

Read the full article in *Cell Metabolism* doi:10.1016/j.cmet.2015.09.005

Testosterone in women: its clinical significance

Testosterone has always been an important chemical messenger in females, and the balance with oestrogen is especially important when it comes to fertility.

This interesting review by Davis & Wahlin-Jacobsen looks at the significance of testosterone deficiency in women and assesses the evidence for its primary replacement use in the context of loss of sexual desire. There is certainly extensive off-licence use of testosterone for such a function. Some clinical trials have demonstrated improvements in cognitive performance and musculo-skeletal health in post-menopausal women. Observational studies suggest that it has favourable cardiovascular effects, according to measurement of surrogate outcomes, but the true risks of cardiovascular disease and total mortality are not as yet established.

Clearly more work on outcomes and safety, and on consistency of testosterone formulations, is required.

Read the full article in *Lancet Diabetes & Endocrinology* doi:10.1016/S2213-8587(15)00284-3

Latitude and effects of GH treatment

Many factors affect the human body's response to growth hormone (GH), and it has often been noted that populations living further from the equator tend to be taller.

De Leonibus *et al.* investigated whether latitude affects the growth rate of children with GH deficiency who are prescribed recombinant human GH (rhGH). Through measuring the growth rate of 118 children from 14 countries for 1 year, they found that this parameter may be the result of a complex gene-environment interaction, with both genetic background and geographic location implicated. Children living further from the equator showed a higher growth response to rhGH. This effect appeared to be related to an interaction between the environmental factor, summer daylight exposure, and genes known to affect growth response to rhGH. Analysis of gene expression networks in these children identified this genetic link, with pathways related to the body's circadian clock (specifically NANOG, the developmental transcription factor) implicated.

This is the first study to observe a gene-environment interaction in children treated with rhGH.

Read the full article in *The Pharmacogenomics Journal* doi:10.1038/tpj.2015.67 (OA)

THE PITUITARY GLAND: ANATOMY, DEVELOPMENT AND PATHOLOGY

WRITTEN BY IAN S SCOTT



The pituitary gland is a vital endocrine organ controlling key aspects of vertebrate homeostasis, clearly justifying its description by Langdon-Brown as 'leader of the endocrine orchestra'. Study of the regional anatomy and developmental biology of the pituitary gland, predominantly in rodent and rabbit models, has revealed many of the mechanisms by which this physiological regulation is achieved, and how adenomas, the most common pathology affecting this gland, support the concept of 'reversible plasticity' of pituitary cells. This brief review addresses selected aspects of pituitary anatomy and developmental biology important in pituitary pathology.

ANATOMY

The pituitary gland (Figure 1) is responsible for maintaining vertebrate homeostasis, regulating processes as varied as somatic growth, response to stress, reproduction, flux through metabolic pathways and lactation. It is composed of two parts, the adenohypophysis and the neurohypophysis.

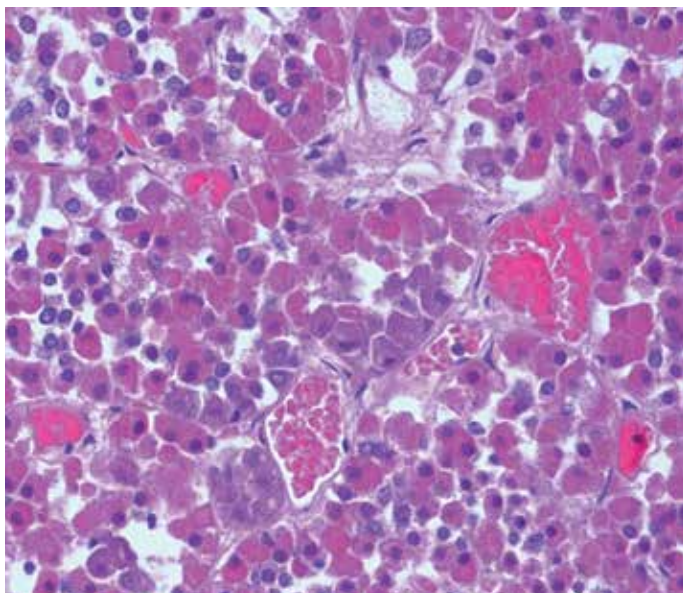
The adenohypophysis forms the bulk of the gland and is composed of three parts: the *pars distalis*, *pars intermedia* and *pars tuberalis*. The neurohypophysis is composed of nerve fibres projecting from hypothalamic nuclei to the median eminence. The pituitary gland is located in the sella turcica, a bony cavity in the sphenoid bone that is roofed by the diaphragma sellae; defective development of which results in the 'empty sella syndrome'.

Nerve supply

The anterior pituitary has no direct nerve supply other than autonomic nerves. The posterior lobe, in contrast, is composed almost exclusively of hypothalamic nerve fibres.

Hypothalamic projections release hormones and trophic factors by neurosecretion into the median eminence and portal system. There are

Figure 1. Normal pituitary gland (haematoxylin/eosin x400). Basophilic and acidophilic cell types are clearly identified. Note the extensive capillary network. ©Ian Scott



two principal tracts; the hypothalamo-hypophyseal tract arises in the magnocellular neurones of the supraoptic and paraventricular nuclei and releases vasopressin and oxytocin into the posterior pituitary, the parvocellular neurones of the tubero-infundibular tract originate in multiple hypothalamic nuclei and project to the median eminence.

Circulatory supply

The adenohypophysis and hypothalamus share a complex portal blood supply carrying trophic and inhibitory hormones from the hypothalamus, thus regulating systemic release of anterior pituitary hormones. The anterior pituitary has no direct arterial supply.

Branches of the superior, middle and inferior hypophyseal arteries supply the median eminence and posterior pituitary. The superior hypophyseal arteries branch into an internal and external plexus. The internal plexus forms glomeruloid structures known as gomitolis. Gomitolis regulate the flow of regulatory hormones in the pituitary paracrine 'biological network' and are the presumed origin of sellar glomangiomas. The inferior arteries supply the pituitary capsule, the neural lobe and the pituitary stalk.

The venous drainage of the pituitary gland is to the inferior petrosal sinuses via the cavernous sinus. The capacity of the venous drainage is exceeded by the volume of blood entering the gland, thus forming a reservoir. Reversal of blood flow here results in secretory products from the adenohypophysis entering the neurohypophysis and median eminence. This vascular anatomy is important in the pathophysiology of apoplexy.

DEVELOPMENT

The anterior pituitary structures derive from Rathke's pouch, an endodermal invagination of the primitive oral cavity. At the third week of gestation, endoderm from the roof of the stomodeum invaginates and, by 6 weeks, the connection with the oropharynx is obliterated. Rathke's pouch then establishes contact with the infundibulum of the hypothalamus.

Early organogenesis is regulated by specific temporal and spatial expression of transcription factors and homeobox genes including the Rathke pouch homeobox (Rpx) protein, Pax-6, and the bicoid-related pituitary homeobox factors (Ptx-1 and Ptx-2). Two members of the LIM-homeodomain transcription factor family, encoded by *LHX3* and *LHX4*, and the P-LIM protein are expressed during Rathke pouch development and mutations are associated with combined pituitary hormone deficiency. An early determinant of pituitary differentiation is the prophet protein (PROP-1).

By mid-gestation, Rathke's pouch is virtually obliterated and is replaced by the pars intermedia. The pituitary portal system forms between 7 and 12 weeks and is fully established by 18–20 weeks. Remnants of adenohypophysis may be deposited along the migration route of Rathke's pouch, the most common site being the roof of the nasopharynx.

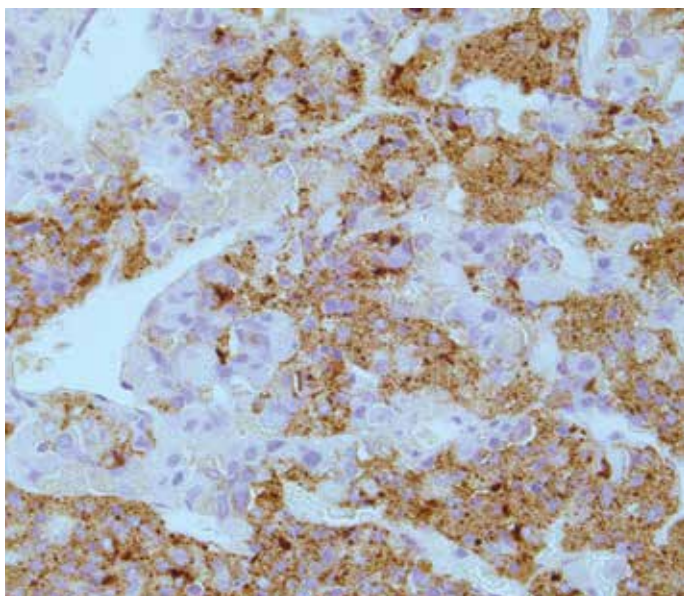


Figure 2. Immunohistochemistry for prolactin (prolactin x400). Note the granular staining in the lactotrophs. ©Ian Scott

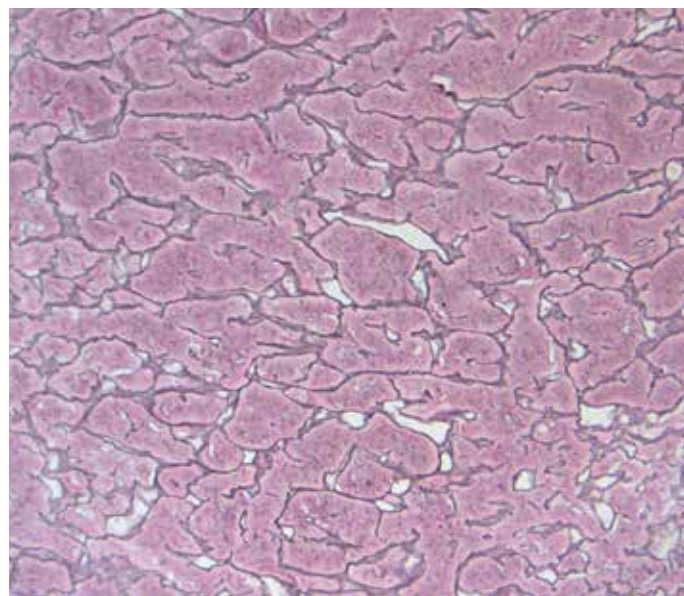


Figure 3. Reticulin network surrounding cell clusters in the normal pituitary gland (reticulin x400). These fibres are lost in adenomas. ©Ian Scott

PATHOLOGY

Pituitary deficiency disorders

Aplasia of the pituitary gland is usually associated with severe congenital malformations. One form, associated with septo-optic dysplasia (SOD), has been attributed to mutation of *RPX1/HESX1* or the *SOX2* gene, but it is clear that other genes remain to be identified. *LHX3* is defective in hypopituitary patients associated with a rigid cervical spine and *LHX4* mutations are associated with combined pituitary hormone deficits in association with Chiari-type malformations.

Pituitary adenomas

Specific immunochemical stains permit differentiation of anterior pituitary cells into somatotrophs (growth hormone; GH), lactotrophs (prolactin; see Figure 2), thyrotrophs (thyrotrophin; TSH), gonadotrophs (luteinising hormone and follicle-stimulating hormone; LH and FSH) and adrenocorticotrophs (adrenocorticotrophin; ACTH). Any of these cell types can give rise to functional or silent adenomas.

Mutations in the *Ikaros* gene and cell cycle proteins are implicated in pituitary tumorigenesis. Pituitary adenomas can be differentiated from normal pituitary tissue by the loss of the nodular reticulin framework (Figure 3) and uniform immunohistochemical staining with a single pituitary hormone.

Adenomas may be hormonally inactive, presenting particularly with visual field defects, headaches, nausea and vomiting. Tumours that secrete hormones often produce clinical symptoms corresponding to the systemic effects of the hormone concerned. Adenomas often maintain some degree of hormonal regulation and pituitary carcinomas are rare, supporting the concept of 'reversible plasticity' in pituitary adenomas. Aggressive behaviour in pituitary adenomas can be predicted by increased expression of the cell proliferation marker Ki67 (Mib-1) or increased expression of the p53 protein.

Diagnosis

Details of individual pituitary adenomas are described elsewhere, but our approach to tumour diagnosis is considered. There is little application for intraoperative smears in pituitary pathology, especially with modern imaging techniques. The exception is where the surgeon suspects hypophysitis, where confirmation of inflammation may limit the extent of surgery.

Our approach is to fix a small fragment for electron microscopy; the remainder being processed for embedding in paraffin. Paraffin sections are stained using haematoxylin/eosin and reticulin. An immunohistochemical panel, composed of synaptophysin, chromogranin A, Cam 5.2, Mib-1, p53, GH, prolactin, ACTH, LH β , FSH β , TSH β and the common α -subunit of the glycoprotein hormones, is then applied. Tissue culture techniques, flow cytometry and molecular analysis have no diagnostic application at this time.

IN CONCLUSION

The pituitary gland is an anatomically unique organ with complex developmental biology and physiology. Defects in differentiation can lead to aplasia or combined pituitary hormone deficiency. Abnormalities in cell cycle regulation result in cell proliferation resulting in hyperplasia, adenoma or carcinoma. Inflammatory and vascular diseases are also encountered. Detailed understanding of pituitary physiology is of vital importance in the management of endocrine disorders.

IAN S SCOTT

Consultant Neuropathologist and Honorary Clinical Associate Professor, Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham

PROLACTIN: THE 'SWISS ARMY KNIFE' OF THE PITUITARY GLAND

WRITTEN BY DAVID R GRATTAN



In the minds of most endocrinologists, prolactin has been 'pigeon-holed' as the hormone that promotes milk production during lactation. Furthermore, hyperprolactinaemia can sometimes be labelled as a straightforward condition that usually responds well to dopaminergic drugs. There seems to be little consequence of not having enough prolactin, and it does not require replacement after pituitary removal.

However, for many years, researchers have been striving to highlight that prolactin has many more functions than just lactation. From an evolutionary perspective, it is an old hormone, present in all vertebrates, most of which do not lactate. In a variety of species, prolactin is involved in functions as diverse as fluid balance, immune regulation, metabolism and behaviour. Prolactin receptors are present in many different tissues, including the liver, gut, pancreas, bone, fat, reproductive tissues and brain. The question is, are any of these other actions of prolactin still important in humans?

In a recent review of the field for *Journal of Endocrinology*'s issue marking '60 years of neuroendocrinology', I highlighted prolactin as a multi-purpose hormone.¹ It is a bit like the iconic 'Swiss army knife': it is pretty clear what its main function is – but then there are many other gadgets whose role is more obscure, until you work out what they do and realise they could be just what you need in certain situations!

Lactation is clearly the main function of prolactin in mammals. But the other functions can play critical roles under specific circumstances. Some complement the main function, while others remain enigmatic. For example, why do males have prolactin?

WHY SO MANY FUNCTIONS?

Prolactin secretion from the pituitary is actively inhibited by dopamine released from the hypothalamus, largely keeping serum prolactin low most of the time. During pregnancy, however, prolactin comes into its own, and the multiple functions become prominent. Mammals have evolved elaborate mechanisms to enable hyperprolactinaemia during pregnancy and lactation. These include production of lactogens by the placenta and/or decidual tissue to activate the prolactin receptor, thereby bypassing the negative feedback regulation of pituitary prolactin secretion.

The hypothalamic feedback itself is remarkably plastic, with



dramatic changes occurring in late pregnancy and into lactation, such that the dopamine neurones show greatly reduced dopamine release, allowing increased pituitary prolactin secretion. Finally, once lactation starts, the act of suckling by the offspring provides the most powerful stimulus to prolactin secretion known. It does this both by maintaining the state of low dopamine output from the hypothalamus, and potentially by adding a stimulatory signal – although if there is a hypothalamic prolactin-releasing factor, we still don't know what it is.

The prolonged elevation in prolactin that is generated by these adaptations is clearly important for milk production, but there are many other actions of prolactin that support this primary role. Lactation requires more than just milk production, demanding behavioural change in the parents, as well as profound metabolic and physiological adaptation in the mother. Almost all of her systems have to function differently to support this new situation, with prolactin co-ordinating an integrated response. It stimulates appetite, suppresses fertility and reduces the stress response and anxiety. It augments insulin secretion and mobilises calcium from bone. It may even alter hair growth to help with temperature regulation. Might abnormalities in prolactin signalling, therefore, underlie various pregnancy complications?

'Prolactin is an old hormone, present in all vertebrates, most of which do not lactate.'

A NOVEL PROLACTIN RECEPTOR MUTATION IN HUMANS

In 2013, an intriguing report in *New England Journal of Medicine*² described a family carrying a novel mutation causing a non-functional prolactin receptor. The three sisters who were heterozygous for the mutation exhibited a range of symptoms, some of which were consistent with our understanding of prolactin function, while others raised new questions. The most obvious phenotype was hyperprolactinaemia, probably due to the loss of the regulatory feedback discussed above. But this explanation was not without controversy, because it was claimed that such feedback has not been proven in humans.³ Ironically, those expressing this doubt seemed to overlook the fact that this study might have provided the very evidence that had previously been lacking!

The second phenotype revealed in this family was a deficiency in fertility. Now, this is where things really got interesting. The women were hyperprolactinaemic, and it is well known that this causes infertility. But if they have non-functional prolactin receptors, how might prolactin be acting to affect fertility? The best explanation would seem to be that prolactin exerts a previously unrecognised positive influence on reproduction in humans,³ as it does in some animals, and that, when this effect was impaired, there were problems with reproduction. So we have more to discover.

APPROPRIATE VERSUS INAPPROPRIATE HYPERPROLACTINAEMIA

The mechanisms by which prolactin inhibits reproduction remain an active area of research. Few of the gonadotrophin-releasing hormone (GnRH) neurones that control reproduction express prolactin receptors, but recent work has highlighted how prolactin might be working indirectly in the brain, through altering activity of kisspeptin or GABA (γ -aminobutyric acid) afferent neurones.

It seems likely that hyperprolactinaemia at an inappropriate time

recapitulates the adaptive responses normally seen during pregnancy or lactation. Infertility is a normal, appropriate response during lactation, but when prolactin is inappropriately elevated, infertility occurs. Potentially, other consequences might also occur during hyperprolactinaemia. For example, patients on anti-psychotic medication (anti-dopaminergic drugs that interfere with the normal regulation of prolactin) suffer not only from loss of libido and infertility from hyperprolactinaemia, but are also at increased risk of metabolic disturbances more characteristic of changes seen in pregnant women.

LOOKING AHEAD

As the hormone responsible for lactation, prolactin has clearly played a critical role in the evolution of mammals. Within this context, it is possible that distinct roles for the hormone have developed in different species, including humans, but it is likely that many common functions remain.

Factors that influence hormone secretion during pregnancy could potentially have consequences for the outcome of the pregnancy on the mother, the offspring or both. Small changes, caused by diet, stress or illness at an inappropriate time, might have effects that do not become apparent until some time later. For example, in mice, suppression of prolactin during early pregnancy causes a decrease in neurogenesis in the maternal brain, and results in postpartum anxiety and impaired maternal behaviour some weeks later. Other diseases of pregnancy and postpartum, such as gestational diabetes or postpartum depression, might similarly have their origins in impaired neuroendocrine responses.

Looking forward, it is an exciting time to be involved in prolactin research. There is a wealth of new research tools available, from genetic approaches conferring the ability to regulate prolactin action in specific cells and tissues, to novel antagonists and antibodies that block prolactin action in clinical trials as potential therapies for a range of disorders and cancers.

Perhaps we will be able to harness the power and utility of nature's 'Swiss army knife' to help us understand the causes of pregnancy complications and to intervene appropriately.

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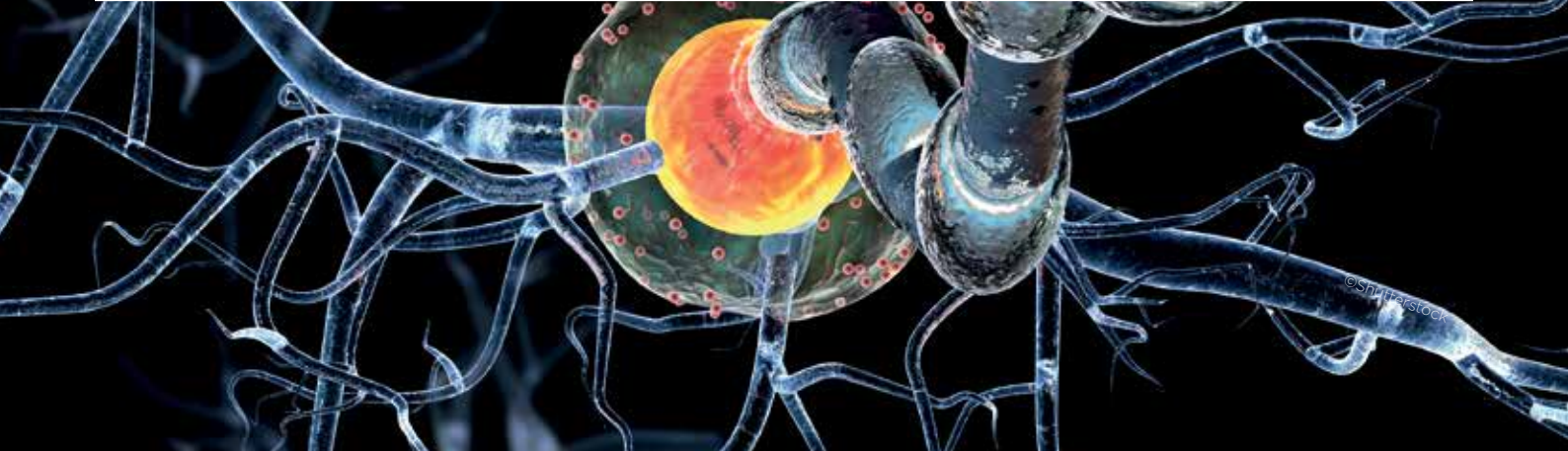


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MY JOURNEY TO BECOMING A PITUITARY SURGEON

WRITTEN BY SIMON CUDLIP



How did I get here? The short answer is luck and circumstances, with a bit more luck thrown in for good measure. The journey also involved food, a love of inappropriate cars, and an appreciation and enjoyment of working with endocrinologists.

I arrived in London, King's College London to be precise, in September 1984, still slightly confused as to how I'd gained a place in medicine. I think what had clinched it was the interview. I'd mentioned that, instead of working for A levels, some of my time in the sixth form had been taken up with part of the British America's Cup Challenge in Newport Rhode Island. One of the panel interviewing me was clearly a sailor, and was deeply impressed by this, in fact so impressed that I was offered a place. I can't remember discussions about exam results or academic achievements playing much of a part in the interview.

Talking to colleagues, this was a feature of interviews in the past. I'm fairly sure one of my peers at medical school was given a place for his musical abilities, perhaps with the medical student review in mind.

FORMATIVE YEARS

I managed somehow to get a grant for a BSc year and spent a blissful year in the MRC Department of Biophysics on Drury Lane, studying immunoparasitology and trying to make a vaccine for malaria. I tried not to feel intimidated by the X-ray diffraction images on the walls outside my lab, and the knowledge that, in the next room, Maurice Wilkins and Rosalind Franklin had unlocked the structure of DNA. Undaunted, I actually did manage to make a vaccine for malaria, murine malaria. Having flirted with the idea of a PhD, I realised my heart was in clinical medicine, and gladly entered the clinical 3 years at King's.

Here, I must make an admission: I'm a closet physician. I realised this during my medical student training, and especially whilst attached to the renowned Liver Unit based at King's. Medicine felt like detective work at times, and I seemed to have an aptitude for it. The surgical firms didn't allow students to become as immersed as the medical firms. The surgical experience was mostly as a second assistant, heaving on a Diva retractor whilst some nervous senior registrar poked around in somebody's abdomen, or peering through the clouds of smoke generated by the diathermy of a perpetually enthusiastic orthopaedic surgeon. It wasn't exactly as inspiring as I'd hoped.

EARLY INSPIRATION

However, I was yet to encounter Professor Edward Howard – and when I did, I was converted. I found myself rather reluctantly dragged to theatre

yet again, probably I thought to witness some heinous act of bowel carnage, with the added bonus of liberal doses of NHS lemon air freshener to counteract the odours. I was fascinated by the scene when I arrived, it was quiet, methodical, calm, and observing the surgeon operating was like watching a master craftsman.

The operation was a complex liver operation for biliary atresia called a Kasai procedure. I'd never seen anything quite like it. Ted (as he was affectionately known) was clearly incredibly gifted, and in perfect control. From that moment, I realised I wanted to be able to operate like that. It was clear that everyone in the operating theatre had complete confidence in what was happening, and his registrar and senior registrar were in awe. I never told Ted he was my inspiration to become a surgeon. In the unlikely event that he finds himself reading an endocrinology magazine in his retirement – thanks!

Surgical senior house officer (SHO) rotations followed round London and Brighton and, as part of this, I found myself in a neurosurgery post at the then Neurosurgical Unit at the Maudsley Hospital in London. To be perfectly honest, it was a bit of an anticlimax. The unit had a slight 'black sheep' feel about it, which I secretly enjoyed, but it lacked the cut and thrust of a busy department, which I'd become used to in my other surgical jobs. What I did like, however, was the nature of the surgery performed, and the patients. It had some of the aspects which I had enjoyed while watching Ted Howard: highly technical surgery performed by skilled surgeons with high stakes. I was hooked and decided that, when I had my FRCS, I'd try and get onto a neurosurgery rotation.

'My suppressed desire to be a physician was sated by the endocrine aspects of pituitary disease, which I find endlessly fascinating.'

FINDING A FOOTHOLD

At that time, this was not an easy matter. Training jobs in neurosurgery were few and far between; I remember, at one point, there were three jobs advertised in single year. A locum post at the Atkinson Morley Hospital (AMH) in Wimbledon beckoned, and it was a pivotal moment. The department and hospital as a whole had a real sense of community and, in the spirit of surgery, a quietly competitive edge. The consultants were all interested in training (a special mention is due to Anne Moore here), and all of the registrars and SHOs benefited from this. In addition, there were two residents from Seattle in the department, adding another dimension and viewpoint which I especially enjoyed.

Pituitary surgery was performed at AMH, but there wasn't a pituitary team, and interaction with the endocrine team (perhaps due to geography) was fleeting. I enjoyed the surgery but, at the time, registrars didn't really get to perform pituitary operations, and spurred on by our American colleagues and their 'go big or go home' approach to neurosurgery, there was an arms race amongst the registrars as to who could do the 'biggest' and the most operations.

MEETING MY MENTOR

Determined to stay in London I then moved to the National Hospital for Neurology and Neurosurgery, Queen Square. It was here I had my first brush with Mick Powell;¹ at the time I wasn't aware that it was going to lead to a friendship and mentorship that has lasted 21 years to date.

In essence, Mick is the reason I'm a pituitary surgeon. One of the many valuable lessons he taught me was if you get on well with people you work with, life is so much easier, and ultimately better for the patients. This was borne out by the willingness of everyone in the hospital to help him and work with him, often beyond the call of duty. When there are three operating theatres running, and only one radiographer to operate

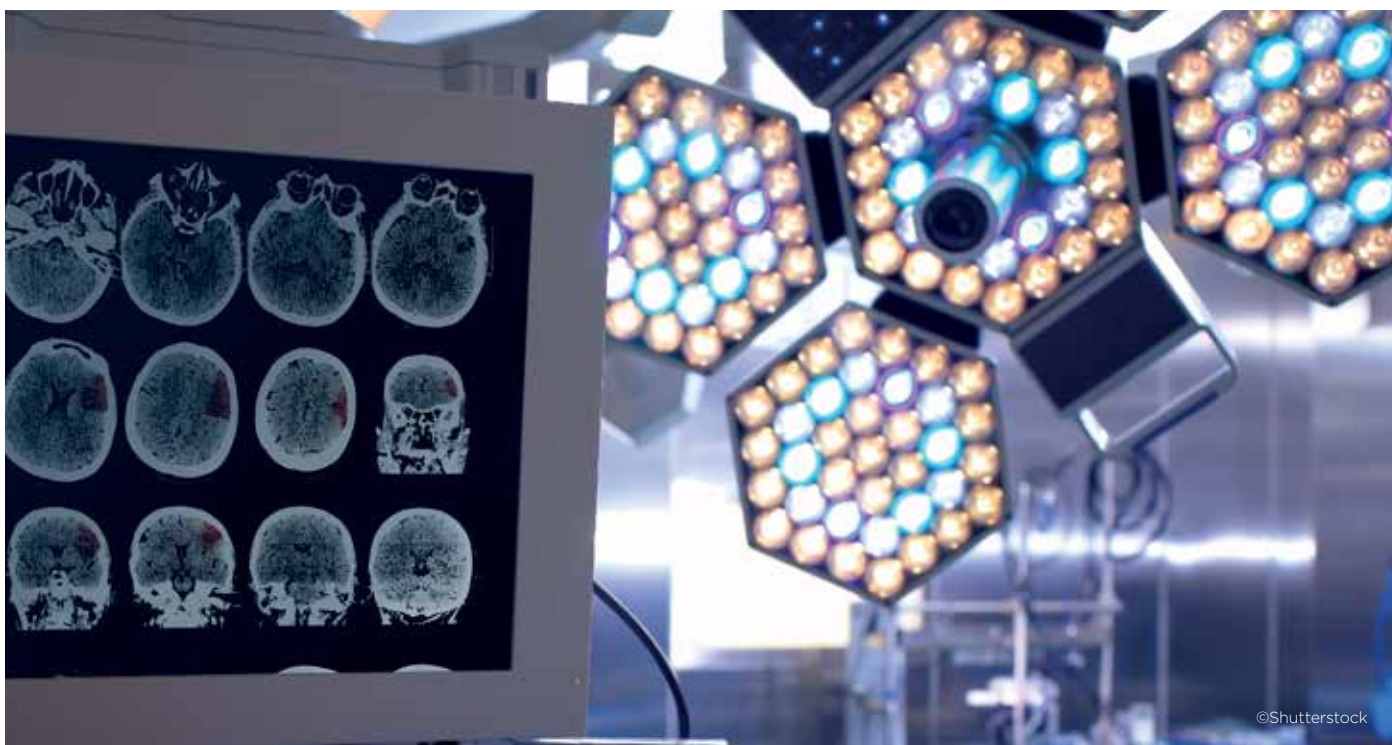
the X-ray machine, the fact that you are popular and well-liked becomes extremely useful.

The fact that he is and was a superb technical surgeon is well known, and I learnt a huge amount over a relatively short time. Another key feature of how Mick worked was his ability to forge relationships with endocrinologists, both professional and social. This extended to regular dinners at his home (he is a superb chef). The joint clinics with endocrinologists were great fun, and very educational. In addition, the patients clearly felt well cared for; sometimes the clinic had the ambience of meeting old friends rather than seeing patients.

'The fact that even small changes in technique, or an obsessive attention to detail, can potentially have a profound effect on outcome means that you are constantly learning and evolving.'

Mick and I also share a love of inappropriate cars and long-suffering wives who tolerate us. International meetings seemed to centre around the quality of the local restaurants and he always knew someone in the locality. In a nutshell, Mick made the practice of neurosurgery 'fun', and it was difficult not to be inspired by his attitude and aptitude.

Shortly after this, I got onto the rotation between AMH and Queen Square, and connived to work with Mick once again when I returned



'My endocrine colleagues keep moving the goalposts, with respect to acromegaly results in particular. It's good to keep the surgical community sharp!'

to Queen Square. By the time I'd finished my training, having squeezed an MD in on the way, I had performed an unusually high number of transsphenoidal operations, and thus, in many ways, the die was cast.

I realise now that this period was slightly artificial. As a senior trainee you are allowed to perform many of the operations, but ultimately share little of the responsibility for the outcomes – a feeling I know only too well as I supervise a fellowship myself. It only really struck home when I spent a further year with Mick in a post-CCT (certificate of completion of training) fellowship, and became much more aware of the outcome of pituitary operations, and how important it is for the surgeon to leave nothing to chance when performing this type of surgery.

CONSULTANCY AND CAMARADERIE

I was very fortunate in being appointed to a consultant post in Oxford at the end of the fellowship with Mick. The post had been advertised following the retirement of Chris Adams, a world-renowned pituitary surgeon. Thus, with some trepidation, my family moved to Oxford. With the importance of building bridges still ringing in my ears from Mick's farewell, I set about establishing myself in Oxford, and to my delight found a like-minded soul in John Wass. We hit it off very quickly, set up a new joint clinic and multidisciplinary team, started meeting every week to discuss patients and generally had 'fun' whilst doing all of this. It was in this period that I really started to learn how to operate.

My suppressed desire to be a physician was sated by the endocrine aspects of pituitary disease, which I find endlessly fascinating. Endocrinology also remains a fundamentally academic discipline, with opportunities for research and collaboration. As you gain experience, it becomes apparent that operations planned with the surgeon, endocrinologist and patients agreeing on the target in the case of microadenomas, and the outcome for macroadenomas, is the way forward. These meetings are always productive. I find if the plan is clear in everyone's mind then life becomes a lot easier.

My current endocrine colleague is the very well known and highly regarded Ashley Grossman. I've been very lucky in Oxford, and I think all surgeons need a strong and opinionated endocrinologist to keep them 'honest'.

REFINEMENT AND REFLECTION

I take my planning a bit further and mentally rehearse and visualise each operation through every small surgical step the night before. It's a bit like watching a movie of the operation, and means I generally have no surprises the following morning. I've heard subsequently that this is a technique used by elite athletes before a big race, although I can't quite bring myself to visualise getting a medal at the end of a successful operation! Having a slightly obsessive attention to detail helps with surgery and I'm probably more obsessive than most.

After every operation I have performed, no matter how good the outcome, I always think 'I could have done that part slightly better'. It may be that a tiny detail like this would have no impact on the patient's outcome, but it's my firm belief that, by adding all these tiny improvements together, I can achieve even better outcomes. This means that, as a surgeon, you can continue to improve throughout your career. The fact that even small changes in technique, or an obsessive attention to detail, can potentially have a profound effect on outcome (e.g. on cortisol levels after surgery for Cushing's disease) means that you as an individual are constantly learning and evolving.

Pituitary surgery also has the ability to satisfy my inner geek. The surgical technique now is quite technologically driven, with high definition endoscopes and screens, neuro-navigation systems to steer your way around the brain like 'sat nav' in a car, fancy drills, instruments and things that go ping!

TRIUMPH IN TEAMWORK

Most surgeons in other disciplines don't have their results externally audited, and the concept of a blood test to prove whether an operation has been successful is a foreign concept to them: I suspect a lot would find it intimidating. I find it hugely rewarding, and the ideal way of improving. After all, if you don't really know how good you are, how can you improve? There is something hugely gratifying about performing surgery and knowing that you are going to fundamentally make somebody's life significantly better.

My endocrine colleagues keep moving the goalposts, with respect to acromegaly results in particular. It's good to keep the surgical community sharp! When I read the agreed criteria for remission, I can't help but think of the line from a Tom Waits song, 'the large print giveth, the small print taketh away.'

'I think my colleagues would agree that, ultimately, it's all about the patients.'

Pituitary surgeons and endocrinologists form a relatively small group, and I enjoy the sense of community and dedication to the task in hand shared between them. This is highlighted at meetings such as the yearly clinico-pathological meeting on pituitary disease in London, and conferences and courses at which I've taught abroad. I come away from these meetings often with a sense that we are all in this together.

Lastly, I think my colleagues in the world of pituitary disease would agree that, ultimately, it's all about patients. Once you've stripped back your reasons for ending up where you are in medicine, it usually boils down to the fact that most find it very gratifying to greet an initially frightened and uncertain patient and their family and be able to offer help.

I still love it.

SIMON CUDLIP

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CONGENITAL HYPOGONADOTROPHIC HYPOGONADISM: A EUROPEAN CONSENSUS STATEMENT

WRITTEN BY RICHARD QUINTON & ANDREW DWYER



Congenital hypogonadotrophic hypogonadism (CHH) is a rare disorder (prevalence 0.025%) caused by absent production, secretion or action of gonadotrophin-releasing hormone (GnRH). It is characterised by incomplete or absent puberty and infertility, in the absence of any structural lesion of the hypothalamo-pituitary region or of broader hypopituitarism.

Around 40% of cases have a 'pure neuroendocrine phenotype', but the remainder exhibit additional non-reproductive defects – most commonly the anosmia that defines Kallmann syndrome (KS). A European CHH consensus statement, with input from clinicians, basic and translational scientists and expert patients was recently published.¹ This includes key elements that merit further dissemination.

ADVANCES IN GENETICS AND PHENOTYPIC ASCERTAINMENT

Perceived until recently in monogenic, Mendelian terms, it is now apparent that CHH is genetically heterogeneous, with over 20 different causal genes so far identified. Many of these genes encode G protein-coupled receptors (GPCRs) and GPCR ligands, and fall into two broad categories. The 'homeostatic' genes are involved in neuroendocrine regulation of GnRH secretion or action, and the 'developmental' genes are involved in embryonic migration of GnRH neurones from the olfactory placode to the hypothalamus (NB 20% arise separately from the neural crest).

Around 60% of unrelated cases carry a disease-associated allele, but most probably also harbour at least another (as yet unidentified) one. There is genetic overlap with other diseases of gonadotrophin insufficiency, comprising CHARGE syndrome (combined pituitary hormone deficiency and hypothalamic amenorrhoea (HA)).

The CHH phenotype is expressed with hemizygous, homozygous or, most frequently, compound heterozygous gene mutations, though monoallelic female heterozygotes are predisposed to functional GnRH deficiency (HA) under conditions of bioenergetic stress.

Several mutations exhibit founder effect, with *PROKR2* L173R being of such ancient lineage that evolutionary advantage must have accrued. A clue arises from women with HA being far more likely to carry this and other CHH alleles than menstruating controls. Ancestral females perhaps survived famine or long distance migration by avoiding pregnancy until environmental conditions became favourable.

Although all series note an excess of male over female cases, there is no genetic basis for this observation; indeed females are equally represented in CHH kindreds. There has probably been ascertainment bias, with CHH men referred to endocrinologists and CHH women instead treated empirically with combined oral contraceptives.

Up to 20% of men with CHH (including those with KS) may achieve normal endogenous gonadotrophin secretion and fertility in later life, but should continue to be monitored periodically as 'reversal' is not always sustained.

MISSED OPPORTUNITIES

Neonatal diagnosis

Mini-puberty in boys, where testosterone and gonadotrophins approach adult male levels, begins in the third trimester and persists for up to 6 months

postnatally. CHH can thus be definitively diagnosed biochemically during this time frame in male neonates with cryptorchidism and/or micropenis. This is all too rarely done.

First contact and transitional care arrangements

Many patients continue to be lost to follow-up and treatment as a result of a poor experience when they first seek medical help in primary care, or as a result of discontinuities between different medical services.

Psychological support

Many men with CHH exhibit high levels of psychological distress: particularly those who experienced intolerable delays in being diagnosed, or in accessing physiological replacement therapy. They should be encouraged to engage with online peer support networks, particularly if access to 'talking therapies' is limited.

TREATMENT RECOMMENDATIONS

Highly effective and simple therapies are available for developing secondary sexual characteristics as well as the induction of fertility in both men and women. CHH is one of the few treatable forms of male infertility. Earliest possible exposure to short term testosterone (or topical local dihydrotestosterone) is recommended for male neonates with micropenis with or without cryptorchidism though, if minipuberty is absent, gonadotrophin therapy may be even more beneficial for its additional stimulatory effect on gonadal development.

If the minipuberty window has been missed, CHH may be challenging to differentiate from simple delayed puberty during adolescence, although a history of micropenis or undescended testes in males and childhood anosmia in either sex is highly suggestive. Brain MRI may contribute, by revealing olfactory bulb hypoplasia or aplasia, sometimes in association with other midline abnormalities. Instead of pursuing a biochemical diagnosis, it is often more practical to commence pubertal induction, with the potential for a subsequent therapeutic pause once final height and pubertal development are achieved.

Pubertal induction and long term replacement therapy in males are generally with testosterone (for which there is no upper age limit). In females, treatment is with 17 β -oestradiol (with systemic or intra-uterine progesterogen as and when required). Dosimetry in adults is guided by serum hormone levels (and also haematocrit in males) and, in the long term, by periodic bone densitometry, initiated once final height is attained.

Fertility prospects are good for men via gonadotrophin spermatogenesis induction and excellent for women (gonadotrophin ovulation induction). However, postcode funding issues remain an issue in the UK, and private providers may be keen to promote more costly *in vitro* fertilisation. Men with severe CHH (testes <4ml and/or a history of cryptorchidism) may achieve better fertility outcomes by reversing the classical order in which gonadotrophins (human chorionic gonadotrophin and human menopausal gonadotrophin) are introduced.

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RADIOSURGERY FOR PITUITARY TUMOURS

WRITTEN BY NICK PHILLIPS



The first line treatment for pituitary tumours, especially those compromising vision by optic nerve or chiasmal compression, is surgery – mainly because it achieves results quickly. The location of the pituitary fossa and pituitary tumours in the skull base, surrounded by important structures, does not favour total excision in all cases, despite great advances in endoscopic surgery. Various types of radiotherapy are used to treat residual or recurrent tumours. Surgery and radiotherapy are complementary, and ultimately achieve control of nearly all pituitary tumours.

A RANGE OF APPROACHES

Radiotherapy for pituitary tumours has some confusing terminology.

Fractionated radiotherapy involves giving a course of radiation treatment every day for about 6 weeks. The dose and treatment regimen is carefully determined to avoid damage to the optic nerve. Fractionated radiotherapy is usually given for relatively large residual or recurrent pituitary tumours that are usually non-functioning, and can't be removed surgically for whatever reason.

Stereotactic radiotherapy involves the use of stereotaxy (a 3D co-ordinate system in X, Y and Z planes) to locate the target with high resolution, and then a course of radiotherapy treatments. This is not often used now to treat pituitary tumours, but may see a resurgence.

Stereotactic radiosurgery was defined by Lars Leksell, a pioneering Swedish neurosurgeon, as the delivery of a single high dose of radiation to a small and critically located intracranial volume through the intact skull. It is mainly used for small residual non-functioning adenomas, and discrete functioning adenomas that can be identified on magnetic resonance imaging (MRI) scanning and are remote from the optic apparatus.

A number of devices are available to deliver a high dose of radiation with stereotactic target localisation (Gamma Knife Perfexion, Cyberknife, and other Linac (linear accelerator)-based devices).

To be clear – stereotactic radiosurgery is not actually surgery. The term was devised to convey the precision of surgery in targeting a small lesion. Radiotherapy (a course of treatment) and radiosurgery (a single treatment) are complementary to one another – each having their own roles – and to surgery.

The advantages of radiosurgery are undoubtedly high resolution and accurate targeting with sparing of normal structures from harmful radiotherapy. Radiosurgery can be targeted to preserve and protect the optic chiasm, the pituitary stalk and the pituitary gland from radiation (Figure 1).

WHEN SHOULD RADIOSURGERY BE USED?

Radiosurgery is the approach of choice when there is a small discrete lesion on MRI scanning that is either a functional or non-functional residual or recurrent adenoma. Higher doses are used for functioning

adenomas, and this means the lesion has to be at least 2mm from the optic chiasm to avoid a dose of radiation to the chiasm.

The latest Gamma Knife radiosurgery machine (Gamma Knife Perfexion) has a particular advantage in pituitary disease in that the cobalt 60 sources are arranged in a toroidal (doughnut-shaped) ring which achieves very accurate dose fall off outside the target area, protecting the optic apparatus. Tolerance doses for the optic apparatus, the pituitary stalk and the pituitary gland are defined, and mean that complications can be minimised.

The aim of radiosurgery for non-functioning pituitary adenomas is to prevent further growth, and most case series report a high control rate approaching 100%, with a high proportion of tumours shrinking over a few years after treatment. Rates of complications are low. A previous criticism of radiosurgery was the lack of robust long term follow-up, and this has now been achieved with some series having over 10 years of study.

Functioning adenomas require higher doses of radiation to treat them. Cushing's disease and acromegaly have better rates of hormonal normalisation than prolactinoma and Nelson's syndrome.

- The primary treatment of acromegaly is surgical excision of the adenoma, and this can be achieved in 50–80% of cases. Repeat surgery tends to be less successful, and this is where radiosurgery has a vital role. The rates of hormonal normalisation increase with time and, at 8 years, approach 60% after radiosurgery.

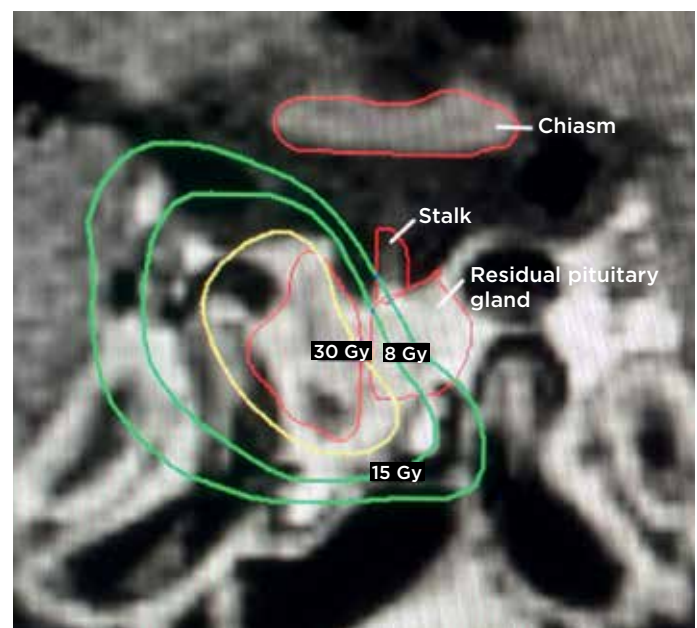


Figure 1. A snapshot from the radiosurgery planning system in coronal section MRI scan. This illustrates the treatment of a small residual non-functioning adenoma in the right side of the pituitary fossa with a relatively well preserved midline pituitary stalk. The green lines illustrate the isodoses of radiation treatment. ©Nick Phillips

- In Cushing's disease, 85% of patients can have hormonal normalisation at 5 years in the best series, with a median time to normalisation of 2 years.
- The control of hormone secretion in Nelson's syndrome is less successful, with adrenocorticotrophin levels only being normalised in about one-third of patients.
- Prolactinoma can be treated by radiosurgery after the failure of pharmacological therapy. The best reported results achieved hormone normalisation of about 50% after 8 years, which is similar to the results of fractionated radiotherapy.

HYPOPITUITARISM AFTER RADIATION TREATMENT

Hypopituitarism can cause significant increases in the mortality rate from cardiovascular disease and is unfortunately a common complication of radiation therapy to the hypothalamic-pituitary axis. Hypopituitarism has been reported in 50–80% of patients 10 years after irradiation.

Hypopituitarism can also develop after radiosurgery. Keeping the total dose to the pituitary gland to a mean of less than 15 Gray can significantly reduce its occurrence (to less than 10%), but long term follow-up is required to ensure the low incidence is maintained.

FINAL THOUGHTS

Radiosurgery has become integrated into the available treatments for pituitary tumours and is complementary to the other modalities, surgery being the mainstay of primary treatment. Small tumours can be targeted with a high degree of accuracy, but there is latency period of several years before success is achieved. Knowledge of the radiation tolerance regarding important structures improves all the time and minimises complications.

NICK PHILLIPS

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Nick Phillips is a radiosurgery practitioner at the Leeds Gamma Knife Centre.

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SHINING A LIGHT ON PITUITARY DISEASE...



WRITTEN BY OLYMPIA KOULOURI & MARK GURNELL

Most endocrinologists will have spent more hours than they care to remember peering at magnetic resonance imaging (MRI) scans, trying to spot the corticotroph microadenoma in a patient with Cushing's disease, or debating whether appearances on a follow-up scan signify post-treatment change/scar tissue or residual tumour. Rather unhelpfully, and just to make things more challenging, a significant proportion of the general population harbour pituitary incidentalomas, raising the possibility of inadvertently targeting the wrong lesion for treatment.

FUNCTIONAL IMAGING

Functional pituitary imaging has been proposed as a means to address these issues, with early studies suggesting considerable promise for the detection of pituitary adenomas.¹⁻³ Different radioligands have been tried, including labelled somatostatin analogues and the commonly used positron emission tomography (PET) tracer ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG).

However, ¹¹C-methionine (Met) has emerged as an alternative PET tracer, with potential advantages in pituitary disease. First, in contrast to ¹⁸F-FDG, it is preferentially taken up by the normal pituitary gland, with relatively low uptake by the surrounding brain. Secondly, most types of pituitary adenoma exhibit enhanced Met uptake, because all share the common property of peptide synthesis.²⁻⁴ Met-PET therefore has potential utility in all subtypes of pituitary adenoma (Cushing's, acromegaly, prolactinoma, thyrotrophinoma or non-functioning tumours).

A major limitation of Met-PET, however, is the lack of anatomical definition offered by PET alone (Figure 1a). Even PET in combination with computed tomography (PET-CT) (Figure 1b) often fails to provide sufficient structural information to inform decision-making with respect to highly targeted therapy (e.g. transsphenoidal re-exploration of lateral sella/cavernous sinus disease, or stereotactic radiosurgery). So the key question arises: how can we combine the anatomical resolution of MRI with the functional information provided by PET(-CT)?

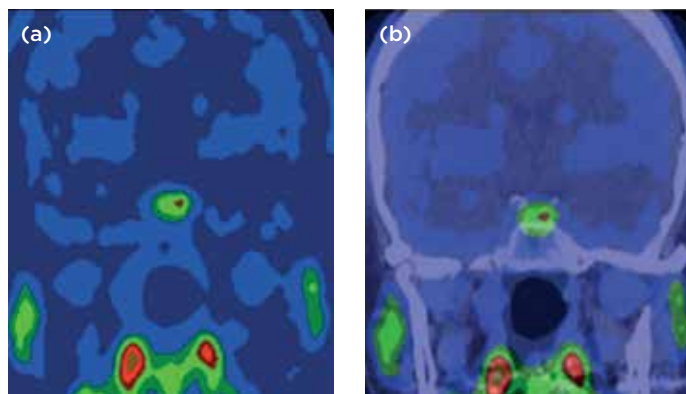


Figure 1. Met-PET at presentation in a subject with a microthyrotrophinoma. (a) Raw PET and (b) PET-CT coronal images demonstrate tracer uptake in the pituitary fossa with apparent increased signal intensity on the left, but lack of clear anatomical definition.

Credit: O Koulouri, M Gurnell

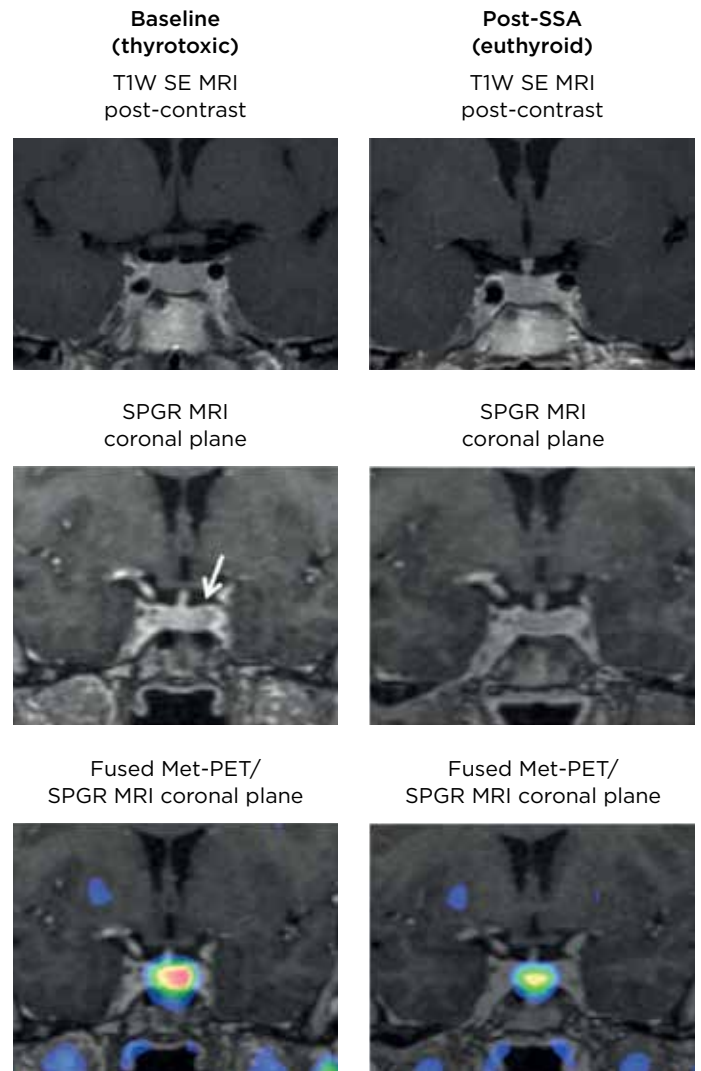


Figure 2. MRI and Met-PET/MRI in the same subject as shown in Figure 1, before and after treatment with a somatostatin analogue (SSA). SE (spin echo) MRI does not reveal a convincing abnormality, but SPGR (spoiled gradient recalled) sequences suggest a possible left-sided lesion. Met-PET/MRI reveals a left-sided 'hot' spot at baseline, which disappears after treatment with SSA. Credit: O Koulouri, M Gurnell

A WINNING COMBINATION

Fortunately, our colleagues in radiotherapy have a ready solution. For years, they have used co-registration of CT and thin slice MRI for radiotherapy planning. Thus, using CT as the ‘bridge’, it is a relatively simple step to co-register PET and MRI images to deliver Met-PET/MRI.

Furthermore, using novel image analysis software, the profile of Met uptake across the sella can now be mapped in greater detail, to aid distinction between physiological uptake by the normal gland and focal uptake by a pituitary adenoma. This technique has two important advantages: (i) it allows the site of maximal Met uptake to be more accurately defined (which can be particularly useful when looking for a small adenoma in an otherwise normal gland), and (ii) it addresses the important question of whether a lesion seen on structural imaging exhibits functional activity or not.⁵

In particularly challenging cases, performing two scans – one at baseline, and a second following ‘endocrine manipulation’ with an agent that suppresses tumoural hormone production (e.g. a somatostatin analogue in thyrotrophinoma or acromegaly) – may provide additional confirmation of the site of a suspected microadenoma or residual tumour by virtue of ‘switching off’ the PET signal (Figure 2).

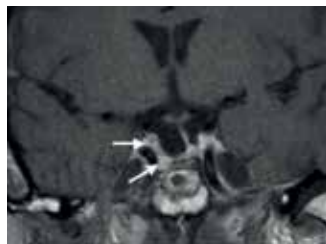
PRACTICAL APPLICATION

Our preliminary findings suggest that Met-PET/MRI may therefore have a particular role to play in:

- (a) confirming/revealing the site of a microadenoma when MRI is inconclusive and surgical intervention is being considered (Figure 2)
- (b) delineating a target for repeat surgery or targeted radiotherapy in post-operative patients with persistent disease but equivocal MRI findings (e.g. residual adenoma versus post-operative change/scar tissue) (Figure 3)
- (c) identifying the site of residual functioning tumour after failed conventional radiotherapy or stereotactic radiosurgery (Figure 3).

So, while MRI will undoubtedly remain the cornerstone of pituitary imaging for the majority of patients, there is now the exciting option of proceeding to functional imaging with Met-PET/MRI for the important subgroup of patients in whom conventional cross-sectional imaging

T1W SE MRI
+ gadolinium



Fused Met-PET/
SPGR MRI coronal plane

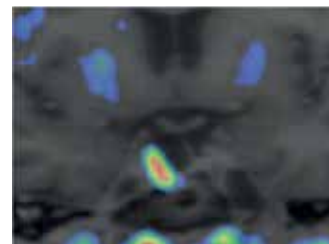


Figure 3. Met-PET/MRI in a subject with residual acromegaly following previous transphenoidal surgery and conventional radiotherapy. SE (spin echo) MRI shows a thin layer of tissue lining the sella. Met-PET/MRI confirms the presence of functioning tissue confined to the right side of the pituitary fossa. Credit: O Koulouri, M Gurnell

is inconclusive, but in whom primary or secondary surgery and/or radiotherapy are being contemplated.

OLYMPIA KOULOURI

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PITUITARY DISEASE IN THE PUBLIC EYE

WRITTEN BY DOMINIC CAVLAN



Clinical endocrinologists, when asked at a dinner party what they do for a living, may explain that is to do with hormones, then, reaching for an example, talk about diabetes, or perhaps the menopause. Recently, the comedian and television presenter Sue Perkins revealed in an interview with *Good Housekeeping* that she has a prolactinoma. This was followed up not only by the national press, but also in many phone calls between endocrinologists and their families, keen to explain that they look after patients with pituitary tumours, ‘...like the woman who presents “The Great British Bake Off”.’

When people in the public eye reveal their medical history it can have a positive impact. The ‘Angelina effect’ describes the measurable improvement in awareness of breast cancer treatment options following Angelina Jolie’s announcement that she had undergone a prophylactic double mastectomy.

The reactions to Sue Perkins’ news illustrated both the positive and negative effects of such stories. Patients with prolactinomas tweeted her describing their own experiences, and found comfort in the way that she underplayed its consequences. Others were angry at the way the news was reported, with criticism of newspapers providing ‘misinformation’ (front page headlines announced that she had a brain tumour). The Pituitary Foundation used the temporary media spotlight to help raise awareness of the services they offer to patients with pituitary disease.

VALUABLE LESSONS

Clinicians can learn from these cases too. Testimonials like those of the opera singer Russell Watson are an important reminder of the impact of pituitary disease on daily life. Watson was diagnosed with a large pituitary macroadenoma in 2008. Following surgery, his tumour recurred and he presented with apoplexy. His descriptions of the cognitive effects of hypopituitarism – ‘I would put the car keys in the fridge’ – are illuminating. He described his experiences to the *Daily Mirror* in 2012¹ as follows.

‘I hate [MRI scans], it puts the fear of hell into me, I relate them to the bad news I’ve had after being in them. It’s like being slid into a coffin and I shake like a leaf. I can walk out in front of 60,000 people and sing “Nessun dorma” no problem, but put me in front of an MRI scanner and the world falls apart. My daughters’ view of me changed massively as a result of being ill; they viewed me as superhuman and all of a sudden I am mortal.’

A ‘HIGH PROFILE’ DISORDER

The most visible celebrities with pituitary disease have been those actors whose acromegaly allowed them to carve out a specific niche in Hollywood. At 7’4” and 500lb, Marian Roussimof was the world’s most famous wrestler in the 1970s, and better known by his stage name of André the Giant. He was too large as a teenager to board the school bus, so Samuel Beckett drove him there on the back of his truck, passing the time discussing their shared passion for cricket. He had a part in Rob Reiner’s fantasy comedy ‘The Princess Bride’ written specifically for him, and remarked that his favourite part of being on set was that ‘nobody stared at me’.

Ted Cassidy portrayed Lurch in ‘The Addams Family’, but his acromegaly also provided him with the booming voice that led to a secondary career as a voice-over artist. Universal Studios attempted to make Rondo Hatton



Clockwise from top left: Russell Watson (@Peter French/Flying Tigers Studio), Ted Cassidy, George Elliott and Sergei Rachmaninov.

a horror movie star in the 1940s, claiming that his appearance was the result of a mustard gas attack in the First World War. Richard Keil remains probably the most famous acromegalic actor after his role as ‘Jaws’ in ‘The Spy Who Loved Me’ and ‘Moonraker’. He also played the title character in the pilot episode of the 1970s TV series ‘The Incredible Hulk’, but was dropped for being insufficiently bulky. He felt that this was no great disaster as, in any case, the green contact lenses that came with the role compounded the visual penalty of his tumour-induced optic nerve damage. Ted Cassidy ensured that acromegaly was represented though, with his aforementioned voice providing the titular Hulk’s trademark roar.

Diagnosing historical figures with endocrine disease can make for a diverting parlour game. Attempts have been made to attribute Rachmaninov’s famously large hands to acromegaly, and much less successful arguments have been put forward that George Eliot’s tendency to undisciplined behaviour and egocentricity were a consequence of growth hormone excess.² A less palatable version of this is in evidence when we observe medical professionals speculating on social media about the medical problems of public figures.

It’s clear that the pituitary gland rarely achieves the front page headlines that its status deserves, but there have been plenty of cameo appearances over the years.

DOMINIC CAVLAN

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Twitter: @domcavlan

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PITUITARY RADIOTHERAPY: TIME TO LOOK AGAIN

WRITTEN BY PETER J TRAINER



In most of the UK, before the availability of high resolution imaging, and when the only post-operative medical therapy was bromocriptine for acromegaly, radiotherapy was routinely administered to patients judged not to have been 'cured' by surgery. The ability to precisely monitor tumour volume, improvements in surgical techniques, the increased array of medical therapies, as well as recognition of the long term complications of radiation, have resulted in fewer patients being referred for radiotherapy.

Hypopituitarism has long been recognised as a near-inevitable consequence of pituitary radiotherapy, but the associated morbidity and mortality were not fully appreciated until the mid-1980s. The move to more selective use of radiotherapy was reinforced by recognition of the associated cerebrovascular complications, particularly in those treated in childhood and early adult life.

However, much of the evidence on which we base our decisions comes from outdated techniques, reflecting an era when planning was conducted without high resolution pituitary imaging, and when there were more uncertainties in the precision of targeting of radiation.

THE PACE OF PROGRESS

The increasing availability of modern techniques has not been fully incorporated into the thinking of many endocrinologists. Approaches include:

- stereotactic radiosurgery (SRS), delivered with sub-millimetre accuracy as a high dose, single fraction on platforms such as the Gamma Knife, CyberKnife and other Linac-based platforms e.g. Novalis Tx
- stereotactic radiotherapy, which delivers conventionally fractionated treatments to the same level of precision
- substantial refinements to 3D conformal radiotherapy, including intensity modulated radiation therapy (IMRT) and volumetric arc therapy (VMAT).

In the USA, where pituitary radiotherapy was historically undertaken less frequently than in the UK, there has been increasing use of the newer technologies. This trend has not been seen in the UK, perhaps partly because the NHS has been cautious about investing in the necessary high cost hardware.

EMBRACING CHANGE

The landscape in the UK is, however, set to change, and endocrinologists must understand and drive the optimal adoption of the various modalities of pituitary radiotherapy, engage in development of national guidelines and resist temptation towards parochial advocacy of local services.

One challenge in ensuring widespread adoption of 'best practice' is the lack of 'marketing' of radiotherapy, so advances rarely reach the greater consciousness. As an endocrinologist in an oncology centre, I can testify that clinical oncologists regularly feel aggrieved that the improved cure rates they achieve for malignancies go largely unrecognised, while claims

by medical oncology colleagues and the industry driving advances in cytotoxic therapies ensure that the media highlight reports of even modest survival benefits.

Lack of promotion of radiotherapy's virtues means it can be forgotten, but the endocrine community must revisit its role in pituitary disease, a process best undertaken in collaboration with clinical oncologists and pituitary surgeons.

THE ROLE OF RADIOTHERAPY

The indications for pituitary radiotherapy are to control tumour growth and hormone hypersecretion. However, with the expansion of the pharmaceutical armamentarium, pituitary radiotherapy has tended to be used only for control of growth, not hormone secretion.

The implication of medical therapy in the absence of radiotherapy is life-long treatment, often with expensive agents. There may therefore be an economic case for pituitary radiotherapy, as it offers the prospect of being able to discontinue such treatment, but any business case should consider the cost of treating hypopituitarism and emerging long term safety data.

CENTRES OF EXCELLENCE

NHS England recently completed an extensive consultation on commissioning SRS services. Recommendations are in the final stages of ratification and procurement is set to commence imminently, with a view to a new service model being operational by April 2016. The initial proposal was that SRS would be restricted to two centres in England and, although this number may increase, the endocrine community must be fully engaged to ensure the selection of centres and techniques is based on best practice rather than vested interests.

The outcomes of surgery are known to be better when undertaken by specialist surgeons with a high throughput, and there is no reason to believe that the same is not true for radiosurgery and advanced radiotherapy. The challenge for endocrinology is to ensure that, whichever centres are commissioned, the service is optimally configured to ensure best practice. It needs to include clear referral criteria, with video-linked, dedicated radiosurgery multidisciplinary teams to allow initial discussion of patients, and clinics that (as a minimum) comprise a specialist clinical oncologist, neurosurgeon and endocrinologist, coupled with a robust system of measuring outcome data. The centres should participate in a unified audit process chaired by a third party.

FURTHER DEVELOPMENTS

The first of two proton beam therapy centres will open in the UK in 2018. Although adult pituitary tumours will not be their priority, pituitary adenomas and craniopharyngiomas are among the current indications for sending children abroad for proton beam treatment, and there is no reason to suggest they will not continue to be indications. The conversation should also encompass multifractional radiotherapy, which will continue to be delivered in many centres, as it is unrealistic to expect patients to travel long distances daily.

There is much to consider, and it is time for endocrinologists, clinical oncologists and neurosurgeons to collaborate in defining modern radiotherapy's place in treating pituitary disease, and to begin prospectively collecting outcome data.

PETER J TRAINER

The Christie NHS Foundation Trust, Manchester Academic Health Science Centre

A PASSION FOR PITUITARY DISEASE

WRITTEN BY JOHN WASS



In the last few years, there have been huge and rapid advances in the treatment of pituitary disease. We now have the ability to render every patient with acromegaly normal for growth hormone and insulin-like growth factor-1. There are new somatostatin analogues for this and Cushing's – albeit that they may be imperfect – as well as increases the numbers of patients who can respond. For Cushing's, this is the first effective medical treatment for the pituitary tumour itself. So, research is rapidly advancing our knowledge and improving treatment options.

Therefore, our knowledge of pituitary disease has hugely increased. We know about apoplexy and that disease recurs in some patients. We know about the natural history of pituitary tumours, particularly macroadenomas, 50% of which enlarge over the next 5 years when untreated. We know the important ways in which craniopharyngioma recurrence can be decreased by post-operative radiotherapy if there is residual tumour. We also understand some of the factors involved in the genesis of this tumour. We know that life expectancy is decreased in patients with Cushing's, even if cured, as well as in those with non-functioning tumours. This is despite the fact that the quality of life (particularly with non-functioning tumours on full replacement therapy) is normal.

Socially, pituitary endocrinologists tend to be a fun-loving, sybaritic crowd with no 'shoulder orifices' [Editor's translation: chips on their shoulders!]. However, the interesting historical aspects of pituitary endocrinology include the rivalry between Andrew Schally and Roger Guillemin, the

Nobel Laureates who discovered the hypothalamic hormones. They published papers within a week of each other relating to the discovery of thyrotrophin-releasing hormone and luteinising hormone-releasing hormone. They didn't even look at each other during the Nobel ceremony!

There remain important advances that need to be worked on. Do dopamine agonists significantly reduce the recurrence of non-functioning tumours? What are the long term histological and other predictors of recurrence of non-functioning pituitary adenomas?

We need to collaborate as endocrinologists more than we currently do, dealing with rare diseases, and we must use NIHR (National Institute for Health Research) funding to the full. We are already working on temozolomide and apoplexy but, for example, does treatment with dopamine agonists during early pregnancy decrease the early fetal loss that is increased in untreated hyperprolactinaemic patients who get pregnant?

We need to encourage young people into endocrinology. Every one of us should accept the challenge of converting the junior doctors in their firm into endocrinologists. We should make sure students are exposed to endocrinology as undergraduates. Our work in this area should never cease – because the next generation is key to our specialty.

JOHN WASS
Professor of Endocrinology, University of Oxford

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'IF THAT'S ALL THERE IS...'

FROM OUR SCIENCE COMMITTEE CORRESPONDENT

Last week, I gave a talk to some fresh-faced students on the mechanisms that control food intake and body weight. Starting from a simple 'in versus out' equation, I ended up with a wiring diagram slide that deliberately had arrows, receptors and lines everywhere: the point being made, or so I thought, that it was good to show complexity.

An earnest young man asked at the end, 'Just wondering, will we ever reach unity in our understanding of energy balance?' Mmm ... tricky. Was he referring to some major state of blissed out consciousness that might descend upon a research scientist after too many hours looking at spreadsheets of calorimetry data? Or was this a knowing reference to something Keanu Reeves said once in 'The Matrix'?

Turns out he just wanted to know if it was likely that, one day, we would know and explain everything about metabolism, having defined and proven a critical all-encompassing central tenet. A reassuring quip about 'eating less and doing more' and we parted.

In the days since, I've been contemplating the scenario of thinking 'all was done, all was known, we've arrived'. I wonder if some 18th century engineers thought they'd hit 'peak science' when steam engines transformed the world. It'd have been pretty hard to consider it worth

splitting an atom to release power when Rutherford's model of the proton and neutron was still the best part of 200 years away.

So what is left to discover? Alas I don't think there is an as-yet-unnamed endocrine gland nestling undiscovered all this time in a crease in the spleen. Equally, I don't believe for a moment that we are 'there'. If we had arrived at 'unity', the disappointment alone would be crushing, never mind the boredom. A certain degree of unknowing is a good thing.

This is not to be confused with bad science, where data and glaring physiological inconsistencies are ignored. I like hearing narratives that invite you in to ask another question, open up an area and suggest more to come. It's all too easy to be bowled over in shock and awe by near-unreproducible studies that vanquish debate and shut down more than they stimulate.

As you travel around reading and listening to science, let us know about people you come across with bright ideas and evolving techniques. We want them to come to our conferences and write for our magazines and journals.

TONY COLL
Science Committee correspondent

GUIDELINES, CREDENTIALS AND PROGRESS

FROM OUR CLINICAL COMMITTEE CORRESPONDENT



Two topics took centre stage during discussions at the recent Clinical Committee meeting. Marie Freel updates you on the latest developments.

SOCIETY GUIDELINE DEVELOPMENT

The Clinical Committee lead on the selection, production and publication of clinical endocrine guidelines within the UK, on behalf of the Society for Endocrinology. Many endocrine disorders are rare diseases without a substantial evidence base, and so clear guidelines written on the basis of available evidence as well as extensive professional experience are invaluable. Society policy for clinical practice guideline production was published in 2014, outlining aims for selection, creation of a working party, guideline development, consultation, publication and dissemination.

The Society collaborates closely with other societies to prevent duplication, such as in the case of the Turner syndrome guidelines currently in development with the European Society of Endocrinology, European Society for Paediatric Endocrinology, Pediatric Endocrine Society (USA), European Society of Human Reproduction and Embryology, and European Society of Cardiology.

In August, the most recent Society for Endocrinology guideline on the evaluation of an infant or adolescent with a suspected disorder of sexual development was published in *Clinical Endocrinology*.¹ This revision of the 2011 guideline was led by Faisal Ahmed (Glasgow) and the Society's Debbie Willis. It is endorsed by a number of relevant professional bodies, including the Association of Clinical Biochemists and the British Society for Paediatric Endocrinology and Diabetes. It provides very clear and

comprehensive guidance on patient selection and evaluation, emphasising the role of the multidisciplinary team, and is equally relevant to both paediatric and adult endocrinologists.

GMC CREDENTIALING

The new General Medical Council (GMC) proposal for 'credentialing' is a process for formally recognising subspecialty competencies. The concept remains at an early stage and requires further development. However, the GMC envisages that all four of the following criteria must be met for a credential to be offered:

- patient need
- service need
- feasibility
- support from authoritative bodies.

The Society for Endocrinology's credentialing working group has agreed, after careful consideration, that bariatric medicine satisfies all four GMC criteria and would be the best candidate for a pilot credentialing scheme. This idea requires further discussion by the Society and the credentialing working group, and further detail is required from the GMC before a curriculum and the regulatory process can be developed. Watch this space for more news...

MARIE FREEL
Clinical Committee correspondent

REFERENCE

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To get in touch with the Society's Committees, email members@endocrinology.org

GET WITH 'THE PROGRAMME'!



What does it take to organise a successful Society for Endocrinology BES conference, providing education, networking and career development opportunities for all our endocrinologists? Here, members of our Programme Committee discuss the rigorous work that goes into putting together a successful conference and how you can have input and get your ideas heard.

The creation of a vibrant and varied Society for Endocrinology BES conference is the task of the Society for Endocrinology's Programme Committee. Endocrinology is an all-embracing discipline with representation from scientists, clinicians, nurses and early career endocrinologists whose interests span all areas of our field.

MEETING YOUR NEEDS

Our aim is to craft a scientifically excellent programme that has something of interest to all members at all times during Society's annual conference. It is of prime importance that we keep in mind the diversity of your interests and experiences, as we evolve the conference into a truly inclusive and expansive event.

The current meeting programme encompasses 12 symposia, 10 'Meet the Expert' (MTE) sessions, 9 plenary lectures, 4 clinical management workshops, nurse and early career sessions, an applied physiology workshop and much more. In total, over 100 invited speakers are chosen by the Committee for the symposia, MTE and other sessions, with an additional 36 short talks selected from the top ranked abstracts. We also identify more than 80 people to chair these sessions, making an effort to include an Early Career representative as well as a more experienced person for each symposium and oral session. The Society's

Conference Team expertly liaises with all these participants to ensure that the meeting runs smoothly.

CHOOSING PROGRAMME CONTENT

Suggestions for the 2015 programme came directly from the Society's Science Committee and Clinical Suggestions Review Group, a full year before the conference. Additional session outlines are received from the Nurse Committee, Public Engagement Committee and Early Career Steering Group.

It is notable that few suggestions for symposia survive the Programme Committee's scrutiny 100% intact, although the underlying concept for a suggested session often remains! Some of our most frequent comments are:

- 'Is this world-leading endocrinology?'
- 'Will people go to that?'
- 'What's new about this?'
- 'Is there a translational angle?'
- 'Will this appeal to both clinicians and scientists?'
- and, most importantly,
- 'Can this speaker give an excellent talk?'

We also pay close attention to the programme of the previous year's conference and try to avoid duplication of topics in successive years. Of late, we have also brought in more overseas speakers, particularly from continental Europe and the Americas, and we feel this has added substantially to the breadth and scientific quality of recent SfE BES

conferences. Our remit is, after all, to expose endocrinologists to the best endocrinology the world has to offer.

MEMBERS' SUGGESTIONS

As the annual SfE BES conference is the main event attended by our membership, we are also keen to receive programme suggestions direct from you, the members of the Society. We would really encourage all members to think about who you would most like to hear talk, and what you would like to learn more about.

If you are keen to discover a certain area, it's a fair bet that many other members will also be interested. It would be worth discussing your ideas with colleagues in your field, as the Committee's experience is that many heads (ideally the whole membership – about 2,500 heads!) are always better than one.

If you can make a suggestion that will appeal to both clinicians and non-clinical scientists, so much the better, but this isn't essential. Suggestions can be made online by filling in a short form on the Society for Endocrinology's website at www.endocrinology.org/meetings/ScientificSessions/index.aspx. Submit your suggestions by Friday 11 December 2015 to be considered for the 2016 programme.

'Your interests ensure we evolve the conference into a truly inclusive and expansive event'

YOUR FEEDBACK COUNTS!

The first item on the agenda for each Programme Committee meeting is the feedback from the previous year's conference. We take your comments and criticisms very seriously, and endeavour to change what we can for the future. SfE BES 2015 was our first conference in a new compact 3-day format: please let us know what you thought, as we continue to grow the conference into an internationally renowned event of scientific and clinical excellence!

SIMON PEARCE, Programme Secretary 2015–2018

CHRIS McCABE, Programme Secretary 2012–2015

ROBERT SEMPLE, Programme Co-ordinator, SfE BES 2015

YOUR CHANCE TO WIN: STUDENT ESSAY PRIZE

Entry to the Society's Student Essay Prize is now open. The Prize is open to both undergraduate and postgraduate students, and provides the opportunity for entrants to have their academic merit recognised by the Society, as well as to win a top prize of £1,000! The application deadline is 11 February 2016 and more details are available at

www.endocrinology.org/grants/prize_studentessay.html

WHY YOU NEED TO NETWORK

WRITTEN BY STEPHEN O'RAHILLY



Our Society's strength is based on the knowledge, experience and drive of you, its members. We are constantly re-examining how we can best harness those qualities to maximise our impact on the science and practice of endocrinology and to deliver services that best reflect your needs.

Recently, we realised the extent to which several of our main committees (such as the Clinical, Science and Programme Committees) were becoming heavily reliant on input from a handful of energetic and committed members. We conceived the Endocrine Networks as a vehicle to improve the two-way dialogue between the membership and the Society.

I hope and expect that the Networks will perform two vital functions.

(a) As a conduit of ideas from members to the key Society Committees and Officers: while never wishing to discourage suggestions from individual members, the Society will inevitably listen more carefully when one of its communities speaks with a single voice.


(b) As a source of ideas for multi-site collaboration in research, education and public engagement: the Networks could propose projects to be catalysed by the Society prior to becoming competitive for external grant support. We have identified funds we can use to support pump-priming of such collaborative projects. We do not provide funding

or direct administrative support simply for the running of a Network, but are willing to look at proposals that help to kick-start a Network.

To launch the Networks rapidly and efficiently, the approach to identifying leads for these groups has, necessarily but unfortunately, been rather 'top down'. We have, where possible, identified a research-active clinician and a basic scientist to act as co-leads, and strived to achieve gender balance and geographic diversity within the UK. It is our intention that, when Network leads complete their terms, their replacements will be identified by the Networks themselves, and that some may acquire international leadership.

The current Networks are Adrenal and Cardiovascular, Bone and Calcium, Endocrine Neoplasia Syndromes, Metabolic and Obesity, Neuroendocrinology, Reproductive Endocrinology and Biology, and Thyroid. I am enormously grateful to the leads and members who are already starting to realise the potential of our Networks. Information on how to join a Network, or to suggest the formation of a new one, can be found at www.endocrinology.org/endocrinenetworks. Please take a look at the website and join up today. Your Society needs you!

STEPHEN O'RAHILLY
President, Society for Endocrinology



Endocrine NETWORKS

Enabling communication, collaboration and knowledge sharing


Endocrine Networks provide dedicated forums across speciality areas within endocrinology. The Networks enable you to communicate with members with similar interests, share best practice, exchange ideas and collaborate on cross-disciplinary research initiatives in Endocrinology.

Grow your NETWORK

Current Networks

- **Reproductive Endocrinology and Biology** - network leads are Professor Stephen Franks and Dr Andrew Childs
- **Metabolic and Obesity** - network leads are Dr Barbara McGowan and Dr Kevin Murphy
- **Adrenal and Cardiovascular** - network leads are Professor Jeremy Tomlinson and Professor Eleanor Davies
- **Bone and Calcium** - network leads are Professor Duncan Bassett and Professor Colin Farquharson
- **Endocrine Neoplasia Syndromes** - network leads are Professor Raj Thakker and Dr Paul Newey
- **Neuroendocrinology** - network leads are Professor Wajit Dhillon and Dr Giles Yeo
- **Thyroid** - network leads are Dr Petros Perros and Dr Carla Moran

Join your network online
www.endocrinology.org





‘Green shoots’ of ENDOCRINOLOGY

WRITTEN BY PASCOE MANNION

In the summer, the Society’s public engagement team hiked out to spread the word of endocrinology amongst the Welsh hills at the Green Man Festival, a music and arts event. Pascoe Mannion, a Society member who volunteered at the event, discusses the benefits to the Society of targeting this type of audience.

For anyone involved in endocrinology, be it as a student, researcher or healthcare professional, it can be only too easy to forget that the majority of the public have no idea what the Society for Endocrinology does. Scientific outreach can be a way of communicating what we do, but how best can we do it?



Scientific outreach events such as Pint of Science and Big Bang Fairs have soared in popularity recently, reaching an audience of tens of thousands every year. Even festivals which have been primarily associated with musical and comedic performances are now getting involved. The Green Man Festival in the Brecon Beacons has led in this with an entire section, ‘Einstein’s Garden’, devoted to scientific outreach.

The limitation of most scientific outreach is that it is targeted at people with a pre-existing interest in science; otherwise they simply would not attend. Offering scientific outreach at a family friendly festival such as Green Man gives us an opportunity to engage both an audience that is already interested in science and one that normally wouldn’t be interested. As well as sparking an interest among students who may go on to work in endocrinology, engaging the public helps to demonstrate the importance of our work to a lay audience. Engendering a perception of endocrinology as an exciting area of research is key to ensuring future support and funding from the public.

Those involved in the Green Man Festival outreach found it a massively rewarding way to spend a weekend, and were surprised by how enthusiastic people were about the research and other work that the Society does. Future involvement in outreach will hopefully be just as rewarding, both for the public and for those spreading the message.

PASCOE MANNION
College of Medical and Dental Sciences, University of Birmingham

MEMBERSHIP SURVEY: WHAT YOU TOLD US...

A few months ago, we asked you about your attitudes towards the Society, the role it plays and the benefits your membership gives you. Some members were chosen randomly to be interviewed by an external research agency. From these responses, we designed a survey that was circulated to the whole membership. We received 194 responses and the results, reported here, were very positive.



Transform your career WITH A GRANT IN 2016

YOUR GRANT, PRIZE AND AWARD PLANNER

Over
£500,000!

Funding provided
by the Society to
members
every year

SOCIETY GRANTS

FOR UNDERGRADUATES...		Apply
Summer Studentships	• £185 per week (up to 10 weeks) plus up to £1,000 for consumables	March
Undergraduate Achievement Awards	• £300 per year for 3 years to an institutional department to encourage excellence in endocrine study	July
FOR UNSPECIALISED SCIENTISTS AND TRAINEES...		
SfE BES Registration Grants	• For clinician, scientist and nurse trainees to attend the conference	July
FOR EARLY CAREER MEMBERS...		
Early Career Grants	• up to £10,000 to progress your career	May & November
Equipment Grants	• up to £10,000 to help establish a laboratory	May & November
Practical Skills Grants	• up to £1,000 for visits to gain skills or experience	Year-round
FOR ALL MEMBERS...		
Travel Grants	• up to £1,100 per year to support conference attendance	March, July & December
NEW! Regional Clinical Cases Meeting Grants	• up to £2,000 to organise a valuable meeting	April & June
NEW! Themed Scientific Meeting Grant	• up to £10,000 to host a cutting-edge scientific meeting	May
Public Engagement Grants	• up to £1,000 to communicate endocrinology to the public	Year-round
Endocrine Network Research Grants	• up to £5,000 to support Society Endocrine Network activities	Year-round

NEW FOR 2016!

REGIONAL CLINICAL CASES MEETING GRANTS

Up to £2,000 each

Support to help you organise informative clinical cases meetings

- Funding available to individuals or institutions
- Any size of meeting supported, anywhere in the UK
- Two grants available

Apply by: 15 April or 15 June 2016

THEMED SCIENTIFIC MEETING GRANT

Up to £10,000 each

Support for you to host a short, cutting-edge scientific meeting

Meeting organisers benefit from:

- Society endorsement
- Help with promotional activities
- Up to £10,000 funding

One meeting will be supported each year

Apply by: 31 May 2016

For further information on all of these opportunities, visit www.endocrinology.org/grants

SOCIETY PRIZES

In addition to the above grants, Society prizes engage students, budding scientists and clinicians within endocrinology:

- Early Career Basic Science Prize Lectureship
- Early Career Clinical Prize Lectureship
- Journal Awards
- National Clinical Cases Meeting Prizes
- SfE BES Early Career Prizes
- Student Essay Prizes

THE ART AND SCIENCE OF PUBLISHING A CASE REPORT: AN EDITOR'S PERSPECTIVE

WRITTEN BY MARALYN DRUCE



©Shutterstock

'If you can't write clearly, you probably don't think nearly as well as you think you do.'

KURT VONNEGUT (1922-2007)

WHY PUBLISH?

There are many reasons why you might wish to write an article for publication. Some of these are altruistic – you may feel the need to make a clear presentation of a complex scientific problem or accomplishment, address a specific hypothesis, provide a route map for others to reproduce your work, or share information to support clinical practice. All of these are worthy goals.

In addition, writing can help you increase your own understanding of a topic, by trying to make sense of it and by conveying it clearly to the reader – as Kurt Vonnegut implies in the quotation above. Moreover, the list of your publications is prized on your CV, job and grant application forms and records of training achieved.

A case report enables you to communicate something new that you have learnt from clinical practice. It could be about an unusual or previously unknown condition, a rare presentation or complication of a known disease, or a new approach to managing a condition. Case reports are the first line of evidence in the medical literature, and provide medical students and doctors with a great opportunity to develop thinking and writing skills.

HOW TO GO ABOUT IT

Any piece of writing needs to start with your intended audience. Who are they and what will they wish to do with the information? Decide early on whether you have a case that is interesting to the general reader (perhaps for the 'easily missed' section of a general journal), a case of cross-over interest (e.g. endocrine oncology for a cancer journal), or a case report that conveys specific endocrine and diabetes learning points for a more specialised audience (such as *Endocrinology, Diabetes & Metabolism Case Reports*).

Read the editorial policy of your chosen journal carefully. Make sure that they accept the kind of report that you wish to submit. Follow their policies and guidance precisely to increase your chances of success.

THREE SIMPLE RULES

You can write a successful case report by following the simple rules of 'Strictly Come Dancing' – choreography, content and execution. The choreography includes knowing and stating the rationale for your case report, including explicit learning points. Have a structure and a story to tell. Make your reader central and include everything that you anticipate they would want to know. Many case report journals provide a template to help you structure your thoughts.

Moving on to content, it is helpful to consider the following questions. Is the content accurate? Are the units correct and consistent? Are the necessary facts present? If you were the supervising consultant or reviewer, what other facts would you ask for? If you don't have them can you get them or say why you cannot? Has your patient given consent? Does the supervising clinician agree? Do you need images, tables, or graphs – would they help or hinder? Have you given enough information for your reader to draw the same conclusions as you? Are your conclusions proportionate? Have you read all of the relevant references and are you sure of their accuracy and quality? Have you omitted any key aspect of background literature and, if you have, can you justify this?

When it comes to execution, you will have already developed a writing style that is natural to you, but you can learn a great deal from ruthless editing by friends, colleagues and seniors. Write naturally, but aim for economy of words. Avoid clichés unless they are necessary and look at each sentence carefully – if you can take out words while retaining the meaning, then leave those words out!

'You can write a successful case report by following the simple rules of 'Strictly Come Dancing' – choreography, content and execution.'

Remember that you are likely to get some rejections along the way and also some suggestions and comments from reviewers. Responding to these is an art, but try to follow their ideas where possible. They are usually aiming to help you improve the quality of your final manuscript.

Then kick back, and allow yourself a pat on the back. You did it!

MARALYN DRUCE

Editor-in-Chief, *Endocrinology, Diabetes & Metabolism Case Reports*

THE ART AND SCIENCE OF PUBLISHING A CASE REPORT: A STUDENT'S PERSPECTIVE

WRITTEN BY SOLOMIS SOLOMOU



As a final year medical student, I got the opportunity to have my endocrinology rotation at Barts in London, one of the most specialised endocrine centres in the UK. All patients at this centre were cases with endocrine pathologies which I had studied during my medical degree, but which I had never previously had the chance to observe in person.

TAKING THE INITIATIVE

I found one case particularly interesting, and thought that this should be published as a case report. As an aspiring endocrinologist, I thought that it would greatly benefit my career progression if I could be the one to write the report, and so I suggested this to my supervisor. To my delight, she agreed. Although she explained that it can be difficult to get a case report published, I was determined to work hard at it.

Over the next few months, I made sure that, whilst preparing for my final exams, I also allowed time to write the report. I felt I learned a lot through this experience. I followed the patient, studied his history and investigations, and learned about his pathology, options for treatment and general management. My understanding had increased after I finished the report and, most importantly, I felt I would be able to apply my knowledge to other patients in the future.

LEARNING THE ROPES

As this was the first time I had prepared a case report for submission, I

was also able to learn how the system works. This included using a journal's format to write the case, dividing it into the relevant sections (abstract, introduction, etc.), and adding references in the journal's style.

Finally, the report was ready for submission, and I felt strangely excited when pressing the submit button. A few weeks later, we received a reply from the journal's editor: the paper had been accepted with minor revisions! I was thrilled; deep inside I had felt that a student would not be good enough to achieve a publication, but I was proved wrong. A student, with good support from supervisors, can create reports of a high standard, suitable for publication.

We made the changes suggested by the reviewers, and a few weeks later the report was published! As the journal is open access, I decided to share my report via social media websites. I was surprised by the amount of interest from fellow students, doctors, medical students from other universities and even the lay public from the UK and other countries. It seemed that a student publishing a case report was not a big deal just for me!

Following this experience, I am very enthusiastic about the prospect of publishing more case reports and other papers in the future.

SOLOMIS SOLOMOU

Foundation Year 2 Doctor, Colchester University Hospital

REFERENCE

Solomou S *et al.* 2014 *Endocrinology, Diabetes & Metabolism Case Reports* EDM130080.



Endocrinology,
Diabetes & Metabolism
CASE REPORTS

YOUR SOCIETY'S CASE REPORTS RESOURCE

The Society for Endocrinology endorses *Endocrinology, Diabetes & Metabolism Case Reports*, a unique, open-access resource that enables practitioners to communicate findings, share knowledge and convey medical experiences efficiently and effectively, furthering both medical education and clinical practice.

As a benefit of this endorsement, members of the Society are eligible for 20% discount on the open access publishing fee (£220 in 2015). To publish your case report, submit it online at www.edmcase reports.com via the easy-to-use article template.

To stay up-to-date with new content, find out about upcoming events and learn more about the benefits of publishing in *Endocrinology, Diabetes & Metabolism Case Reports*, sign up to receive our bimonthly newsletter: http://bit.ly/EDMCR_News

DON'T MISS THE ENDOCRINE POST!

The Society for Endocrinology's new blog

To hear more on Society initiatives and updates from the world of hormones, visit <http://endocrinologyblog.org>

LONDON'S FIRST STUDENT-LED ENDOCRINOLOGY SOCIETY

WRITTEN BY JAYANI SURIYAKUMARAN



©Shutterstock

There is no better way of declaring your love for a sport, hobby or even specialty than by joining a university society dedicated to it. And if one doesn't exist, then create it!

In September 2014, six fourth year students, including myself, decided to set up a society to share our passion for endocrinology with other students from Barts and the London School of Medicine and Dentistry. We sought help from the wonderful Dr Maralyn Druce at the Barts Endocrinology Department to help us submit the necessary application form.

WHAT KINDLED THE FLAME?

The six of us who formed the founding committee were introduced to the specialty during our intercalated degree in molecular therapeutics, when we completed the neuroendocrinology module. The course was extremely well organised, and we got a real flavour of endocrinology through being invited to meetings and clinics. So, 2 years after being welcomed so warmly by the Endocrinology Department, we felt other students would benefit from having the same taste of endocrinology that we had experienced.

FIRST STEPS

Other than our desire to share the wonders of endocrinology, we had no idea what events we would host, or whom we would invite to host them. We returned to Dr Druce and asked whether she would kindly be our Staff President (a senior member of staff within the medical school who oversees the activities of the society). She helped us brainstorm ideas for events, and the committee decided to host four events during the academic year.

The Freshers' Fair was our first platform to promote the society. We cast our net by advertising a prize draw for the first 20 students who signed up, and the prize was an endocrinology textbook or the *Oxford Handbook of Clinical Medicine*.

A tiring afternoon saw us striving to convince nearly 200 students that paid membership to the endocrinology society would allow them exclusive access to lectures by renowned speakers and the chance to network with pioneers in lab-based research at the Centre for Endocrinology (William Harvey Research Institute). We persuaded about 150 students to sign up to the society – and approximately 10 students to pay for membership.

When we submitted the society application form, we promised the student union a minimum of 20 members, secretly believing we would at least double that number. So, it was slightly demoralising to have only recruited 10 members so far.

ONWARDS AND UPWARDS

Our first society event took place exactly a month later. We started promoting it early, to achieve maximum turnout. It was delivered by our own Staff President and entitled 'Neuroendocrine tumours: meet the family', reflecting our speaker's special interest and enabling us to introduce this exciting family of tumours that were not taught in the curriculum. A very good turnout saw nearly 50 students attend, including a handful from other universities.

Our second event was on 'Hormones and doping', with speaker Dr Craig Stiles, a Senior Registrar from Barts and the London Endocrine Department, who has a keen interest in the subject, especially as he is an avid cyclist. The event attracted attendees interested in sports medicine as well as those wishing to learn more about doping. We organised this event in collaboration with the London Sports and Exercise Medicine Group.

Our subsequent networking event was hugely oversubscribed. It was a fantastic opportunity for students to meet consultant endocrinologists and to inspire attendees to get involved in summer projects, audits, etc. It was very rewarding, since many students benefited from the evening, and members of staff enjoyed it as well.

A YEAR OF SUCCESS

Our final event of the year was based on the past, current and future treatment of diabetes, delivered by Dr Tahseen Chowdhury, a consultant diabetologist. A lot of our members expressed an interest in holding this event, since a large proportion of the local population suffer from the condition. As with previous events, this one was also very well received.

By June, we had accumulated about 80 paid members, which was definitely a great success! The new committee was elected in the same month and all responsibilities have now passed to them.

We hope to see our endocrinology society grow into a bigger, even more successful organisation, and that it collaborates with new student endocrinology societies across the UK. Since our last event, we have been asked by students at other medical schools how we did it, so here is our success story – good luck creating yours!

JAYANI SURIYAKUMARAN

4th year MBBS Student, Barts and the London School of Medicine and Dentistry

The founding committee of Barts and the London Endocrinology Society was: Jayani Suriyakumaran and Sanjiv Yogarajah (Co-Presidents); Minolhini Ravendran (Treasurer); Writaja Halder (Events Co-ordinator); Rea Ganatra (Secretary); Mina Al-Janabi (Clinical Representative).

FIND OUT MORE ONLINE:

- How to take your place as a Student Ambassador
- Find your local Student Ambassador
- How to set up your own university endocrine society

See www.endocrinology.org/careers/student

And remember, you can get involved whether you are a medic or a scientist!

NEW MASTERS LEVEL MODULE IN ADULT ENDOCRINE NURSING



WRITTEN BY ANNE MARLAND

I am delighted that the Society for Endocrinology has secured a partnership with Oxford Brookes University to provide a work-based learning module in adult endocrine nursing. This is the first of its kind in the UK and Europe.

Over a decade ago, the Society developed a Certificate of Adult Endocrine Nursing, to help endocrine nurses validate their practice, knowledge and experience. The Certificate is awarded to nurses who submit an evidence portfolio that is assessed by senior members of the Society's Nurse Committee. Currently, the Certificate has no academic accreditation and, therefore, is not easily transferable.

Within the current professional climate, with revalidation looming and evolution of nursing practice, the focused disciplinary trajectory of the nursing profession is academic. Therefore the Society for Endocrinology was passionate about providing a new academic pathway for our wonderfully dedicated nurses. As you are aware, the Society is committed to attracting and retaining high quality nurses to work in endocrinology to improve science and medicine for the public benefit. Indeed, we are at the forefront of advanced practice globally.

Through this new partnership, the Society aims to motivate endocrine nurses to engage in postgraduate study to further their clinical and educational development. This will ultimately result in more highly skilled and academically competent professionals.

WHAT WILL THE MODULE COMPRISE?

The following is an extract from our initial publicity material: 'Registered nurse members of the Society for Endocrinology who have successfully completed a portfolio based around the Society's Competency Framework for Adult Endocrine Nursing may wish to gain academic recognition of their achievements. Successful completion of the module leads to the conferment of 20 Masters level credits (level 7) by Oxford Brookes University, which can be counted towards the University's MSc in Health Sciences, or towards other Masters level qualifications at Oxford Brookes and elsewhere.'

'The Society aims to motivate endocrine nurses to engage in postgraduate study, to further their clinical and educational development.'

Accreditation will allow the certificate holder to transfer APEL (accreditation of prior experiential learning) academic credits to a wide range of higher education options in the UK and overseas. Students registering for the module are asked to prepare and submit a reflective portfolio demonstrating sustained critical engagement with the Society's Competency Framework. The portfolio should support the claim that students are competent in all of the specified areas and proficient or expert in selected specialist areas.

Addressing each appropriate competency and standard in turn, a reflective essay of 2,500 words should identify key areas of learning and development, and areas for nursing research, service development and practice development. Indicative activities might include: introducing

a nurse-led clinic, compiling a patient information sheet or developing outreach services. There are also compulsory elements, such as attending the Society BES conference and Endocrine Nurse Update, submitting abstracts and making oral presentations.

STUDENT SUPPORT

The student will have the opportunity to liaise with the academic tutor in respect of any academic writing development needs. They can contact the work-based learning facilitator regarding any content-specific queries relating to the Society for Endocrinology. This is most likely to be the clinician working alongside the student or a suitably qualified peer. All the supporting material will soon be available.

You may have discussed this exciting initiative with Nurse Committee representatives at the recent Society for Endocrinology BES conference. We will have a dedicated session on the subject next year at Endocrine Nurse Update (Birmingham, 21–22 March 2016).

I'm really looking forward to the future and to this exciting development for endocrine nurses. This course will enable you to differentiate your role within your clinical environment, demonstrate a strong emphasis in clinical leadership, advance your clinical practice, develop your professional career and enhance your knowledge of research and evidence-based healthcare, through analysis of service delivery models.

Good luck to all of you who wish to advance and consolidate your practice.

ANNE MARLAND

Advanced Nurse Practitioner in Adult Endocrinology,
Oxford University Hospitals NHS Foundation Trust

LISA SHEPHERD

NURSE COMMITTEE CHAIR



I am delighted that this issue brings news of an exciting development brought about by a working party of the Nurse Committee. As you may know, the new Masters module in adult endocrine nursing was launched at the recent Society for Endocrinology BES conference.

Nurses working in endocrinology have always been encouraged to complete the Society's Certificate in Adult Endocrine Nursing as part of their continuing professional development. It has also been used as a marker of experience and competence for departments when recruiting to endocrine nurse specialist posts. That the Certificate has now been developed into a MSc work-based learning module, through a partnership between the Society and Oxford Brookes University, is tremendous news.

I thank Anne Marland from Oxford for her explanation of the Masters course, and I look forward to the first students undertaking the module. In the meantime, I wish you all a very merry Christmas and a happy new year.

LISA SHEPHERD

18TH ANNUAL CLINICOPATHOLOGICAL CONFERENCE ON PITUITARY DISEASE

London, UK, 25 February 2016

Focusing on a multidisciplinary approach to pituitary disease, this event at the Royal College of Obstetricians and Gynaecologists will see keynote speakers, poster rounds and discussion of challenging cases by endocrinologists, neurosurgeons and radiologists, amongst others. It is suitable for consultants and trainees at all levels, as well as clinical nurse specialists.

To register, visit <http://bit.ly/1Rin2ew>, or for more information, contact conference organiser Stephanie Baldeweg at stephanie.baldeweg@uclh.nhs.uk

EUthyroid: NEW PAN-EUROPEAN STUDY OF IODINE DEFICIENCY

EUthyroid is a major new European initiative that aims to examine iodine deficiency prevention measures across the continent.

There is currently no harmonised measure across the EU to ensure that citizens' iodine intake is sufficient to prevent health problems. This programme will compare national iodine measures and examine dietary habits to work out appropriate methods to improve iodine intake across Europe. In particular, the study will focus on the iodine intake of pregnant women and the impact of any deficiency on the development of the child.



Its budget of €3 million is funded through the EU Horizon 20:20 programme and comprises 31 partners from 28 countries. You can find out more at <http://euthyroid.eu>

WHAT'S NEW FROM THE PITUITARY FOUNDATION?

The Pituitary Foundation is the UK's national support and information organisation for pituitary patients, their families and friends. The Foundation runs a number of initiatives that clinicians will find useful:

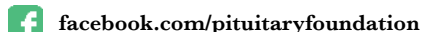
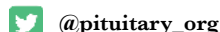
- **Endocrine clinic resource packs** – these new packs provide a tailored selection of the Foundation's leaflets and resources to help clinics educate patients and enable them to self-manage their condition (order at <http://bit.ly/1VGRHDD>)
- **Endocrine specialist nurse helpline** – a unique and confidential service offers patients phone access to a specialist nurse who will provide medical advice
- **Resource library** – clinics and patients can order a range of booklets covering conditions and procedures, information for healthcare professionals and the wellbeing/lifestyle of pituitary patients from the Foundation's website
- **National Pituitary Conference for patients** – this enables patients to learn more about pituitary conditions from experts and to meet one other. Held annually, the next is in Leeds on Saturday 23 April 2016.

HELPLINES

Email support helpline@pituitary.org.uk
Patient information 0117 3701320 (Mon–Fri 10.00–16.00)
Endocrine nurse 0117 3701317 (Mon 10.00–13.00 & 18.00–21.00; Thu 09.00–13.00)

GENERAL INFORMATION

www.pituitary.org.uk



ADDISON'S MEDICAL RESEARCH GRANT

The Addison's Disease Self Help Group invites applications for its 2016 medical research grant.

The grant is for up to £5,000 to assist with equipment, laboratory charges and similar project running costs. Research projects must be purposed towards advancing clinical practice in the management of Addison's disease and steroid-dependence.

If you are interested, please email info@addisons.org.uk to request a copy of the application form or visit <http://bit.ly/1PL6y0K>

ENDOCRINE NURSE UPDATE 2016
 21 - 22 March 2016
 Hilton Birmingham Metropole Hotel, NEC, Birmingham
www.endocrinology.org/meetings

Society for Endocrinology

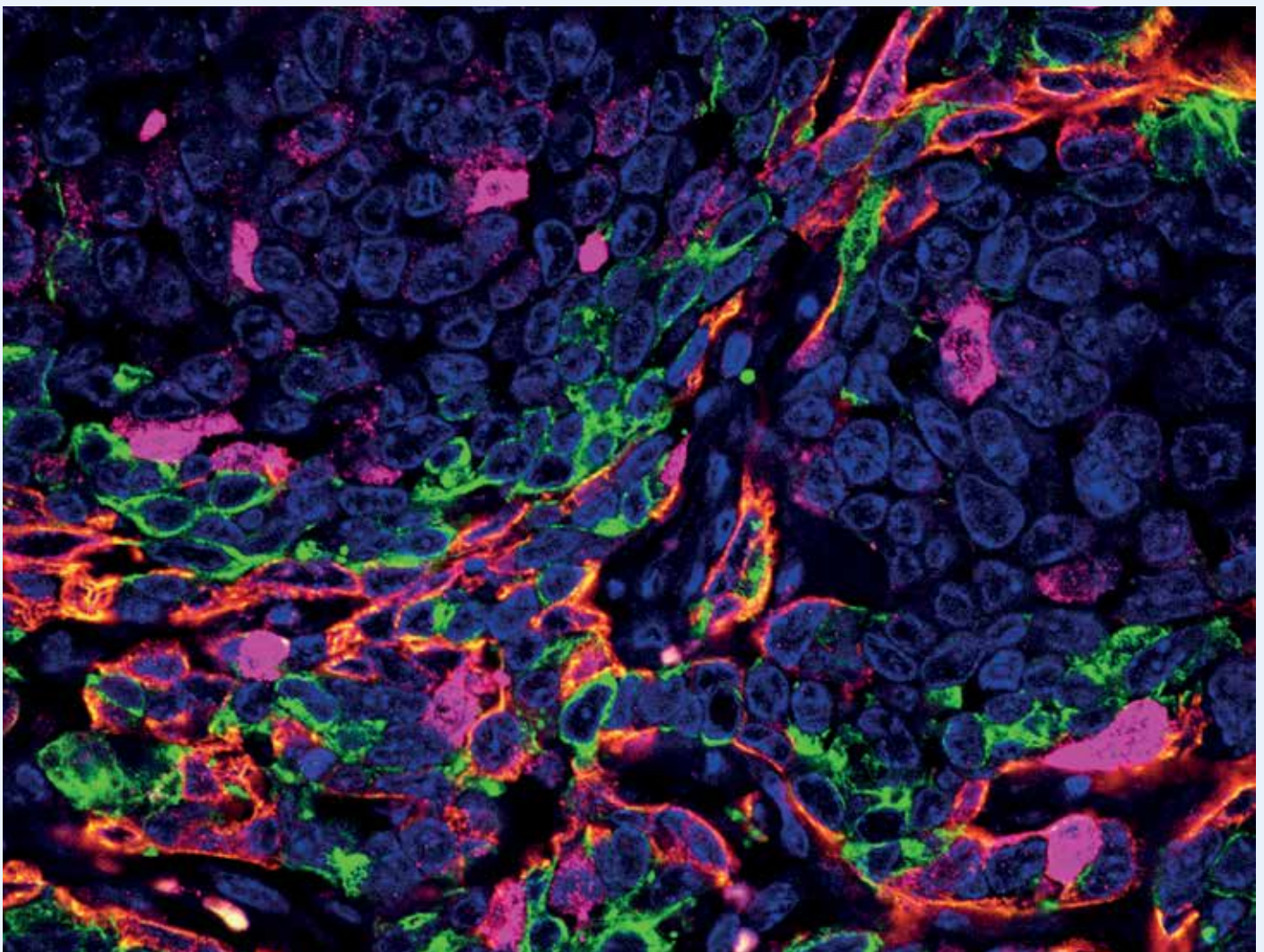
Images in **ENDOCRINOLOGY**

Here is the latest highlight from our journal Cover Art Competition, showcasing the best images in endocrinology.

COVER IMAGE FROM *ENDOCRINE-RELATED CANCER*

DECEMBER 2015

The image depicts a TP53-null mammary tumour immunostained for cytokeratin 8 (green), cytokeratin 5 (red) and Wnt-active stem cells (pink). Nuclei were counterstained with DAPI (blue). Credit: *K Roarty; this image was acquired in the Integrated Microscopy Core at Baylor College of Medicine using a Nikon A1R-s confocal microscope (funding sources: NIH HD007495, DK56338 and CA125123).*



Enter our Cover Art Competition

for *Journal of Endocrinology*, *Journal of Molecular Endocrinology* and *Endocrine-Related Cancer*.

Visit www.endocrinology.org/news for more information.

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Presentation: Tostran 2% Gel, contains testosterone, 20 mg/g. **Indication:** Replacement therapy with testosterone for male hypogonadism when testosterone deficiency has been confirmed by clinical symptoms and laboratory analyses. **Dose:** The starting dose is 3 g gel (60 mg testosterone) applied once daily to clean, dry, intact skin, on the abdomen or to both inner thighs. Adjust dose according to clinical and laboratory responses. Do not exceed 4 g of gel (80 mg testosterone) daily. Apply after washing, bathing or showering. Do not apply to the genitalia. Do not use in women, or children under the age of 18 years. **Contraindications:** Known or suspected carcinoma of the breast or the prostate. Hypersensitivity to any of the ingredients. **Special warnings and precautions for use:** Not to be used to treat non-

specific symptoms suggestive of hypogonadism if testosterone deficiency has not been demonstrated and if other aetiologies have not been excluded. Not indicated for treatment of male sterility or impotence. Pre-examine all patients to exclude a risk of pre-existing prostatic cancer. Perform regular monitoring of breast and prostate. Androgens may accelerate the development of subclinical prostatic cancer and benign prostatic hyperplasia. Oedema with/without congestive heart failure may be a serious complication in patients with pre-existing cardiac, renal or hepatic disease. Discontinue immediately if such complications occur. Use with caution in hypertension, ischaemic heart disease, epilepsy, migraines and sleep apnoea as these conditions may be aggravated. Care should be taken with skeletal metastases due to risk of hypercalcaemia/hypercalcaemia. Androgen treatment may result in improved insulin sensitivity. Inform the patient about the risk of testosterone transfer and give safety

instructions. Health professionals/carers should use disposable gloves resistant to alcohol. **Interactions:** Androgens can increase the anticoagulant effect of anticoagulants. Concurrent administration with ACTH or corticosteroids may increase the likelihood of oedema. **Side-effects:** Very common: application site reactions (including pruritis, atrophy, pruritis, rash or erythema). Common: increased haemoglobin and haematocrit, increased male pattern hair distribution, hypertension, gynaecomastia, peripheral oedema, increased PSA. May cause irritation and dry skin. Consult SPC for further details of side-effects. **Pack Size and Price:** Packs containing one or three 60 g metered-dose canisters per pack. Price £26.57 per canister. **Legal Category:** POM. **Marketing Authorisation Holder:** ProStrakan Limited, Gofabank Business Park, Galashiels, TD1 1QH, UK. Marketing Authorisation Number: PL1650E/0025 ©ProStrakan. ®Registered Trade Mark. Date of PI Preparation: November 2013.

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Adverse events should also be reported to ProStrakan Ltd on 01896 664000.

References: 1. Tostran[®] Summary of Product Characteristics, June 2010. 2. Testogel[®] Summary of Product Characteristics, November 2006.
Date of preparation: February 2014. Job code: M015/1224

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